Effects of a Single Session of Aerobic Exercise on Cognitive Function among Patients with Chronic Stroke

by

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Author's Declaration

I hereby declare that I am the sole author of this thesis. This is a true copy of the thesis, including any required final revisions, as accepted by my examiners.

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Abstract

The incidence of stroke is increasing and is expected to continue to increase with the aging population, escalating rates of obesity and physical inactivity, and the rising prevalence of heart failure. Stroke is a leading cause of long-term disability, which includes approximately half of survivors that experience cognitive impairment. It is accepted that aerobic exercise can improve physical health in both healthy and stroke populations. Evidence also suggests aerobic exercise may positively affect cognitive function among healthy adults; however, whether there are similar beneficial effects among stroke survivors remains unclear. The purpose of this thesis was to examine whether a single session of moderate intensity aerobic exercise acutely improves cognitive function, specifically executive function, in comparison to a rest control among people with chronic stroke. Our first objective was to determine whether aerobic exercise alters cortical processing, as measured by P300 amplitude and latency during a modified Eriksen Flanker task. The second objective was to investigate whether aerobic exercise influences behavioral measures of response time and accuracy during a modified Eriksen Flanker task. Finally, the third objective was to examine the time course of effects up to 40 minutes after exercise cessation. In our sample, participants had shorter P300 latency and larger P300 amplitude 20 to 40 minutes after exercise cessation in comparison to rest. There were no significant behavioural changes. These findings suggest that aerobic exercise may enhance, or at least maintain cognitive processing speed and attention 20 to 40 minutes after exercise cessation, which otherwise deteriorated in the rest condition. Although results should be viewed cautiously due to a small sample size, these findings have potential implications for stroke rehabilitation. Our results suggest that aerobic exercise may be able to improve attentional focus during subsequent rehabilitation exercises for up to 40 minutes or more. Future research should examine whether

the effects of various exercise doses and whether paired exercise and rehabilitation improves clinical outcomes.

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List of Acronyms

ADLs: Activities of Daily Living

ARAT: Action Research Arm Test

BDNF: Brain-Derived Neurotrophic Factor

CEP: Certified Exercise Physiologist

CMSA: Chedoke-McMaster Stroke Assessment

DA: Dopamine

ECG: Electrocardiogram

EEG: Electroencephalography

ERP: Event-Related Potential

GLU: Glutamate

HRmax: Maximal Heart Rate

HRR: Heart Rate Reserve

MoCA: Montreal Cognitive Assessment

NE: Norepinephrine

RPE: Rating of Perceived Exertion

VO_2 max: maximal aerobic capacity

1.0 Introduction

Stroke is a leading cause of long-term disability and is associated with significantly lower quality of life (Gordon et al., 2004; Hochstenbach, Anderson, Van Limbeek, & Mulder, 2001). Cognitive impairment is estimated to occur in over half of those that survive a stroke (Patel, Coshall, Russ, & Wolfe, 2002). Evidence suggests that a single session of aerobic exercise may positively affect cognitive function in healthy young and older adults, yet the effects of exercise on cognitive function in stroke are poorly understood. Therefore, the purpose of this study was to determine the acute effects of a single bout of aerobic exercise on cognitive function, specifically executive function, among stroke survivors. The duration of effects was also examined. This will have practical implication of informing referral and treatment practices for exercise after stroke to optimize rehabilitation outcomes. The literature review of this thesis will discuss the epidemiology and pathology of stroke, physical and cognitive impairment after stroke and corresponding rehabilitation practices. A summary of prior literature regarding exercise and cognitive function in stroke as well as healthy adults is also presented.

2.0 Literature Review

2.1 Epidemiology of Stroke

Approximately 50 000 persons in Canada (HSF, 2013) and 795 000 persons in the United States (Roger et al., 2012) experience a new or recurrent stroke every year. First attacks account for roughly 77% of strokes and recurrent attacks consist of the remaining 23% (Roger et al., 2012). Of those that experience a stroke, approximately 15% die, 10% completely recover, 25% are left with a minor impairment or disability, 40% suffer moderate to severe impairments and 10% require long-term care because of such severe disablement (HSF, 2013). The death rate due to stroke is declining, but the incidence of stroke is increasing (Feigin, Lawes, Bennett, & Anderson, 2003). Due to the aging of the population; epidemics of diabetes, obesity and physical inactivity; and increasing prevalence of heart failure, the incidence of stroke will likely continue to increase over the coming decades (Gillum & Sempos, 1997). As a result, it is estimated that by 2030, the incidence of stroke will increase by 21.9% (Go et al., 2013). Declining stroke mortality rates combined with increasing incidence of stroke will result in a larger number of persons living with chronic stroke-related cognitive or physical impairment. Stroke is already one of the leading causes of long-term disability (Gordon et al., 2004) and thus, optimizing stroke rehabilitation practices warrants further study.

2.2 Risk Factors for Stroke

There are non-modifiable and modifiable risk factors of stroke (Goldstein et al., 2001). Non-modifiable risk factors include age, race, gender and family history (Goldstein et al., 2001). Modifiable risk factors can be classified into two categories, disease or health condition risk factors and behavioural risk factors. Disease risk factors that may be modifiable by treatment

include non-valvular atrial fibrillation, asymptomatic carotid stenosis, coronary artery disease, heart failure, peripheral arterial disease and sickle cell disease. Additional health conditions that can be modified by treatment include hyperlipidemia, high total cholesterol, low HDL cholesterol (<40mg/dl), diabetes mellitus and hypertension (Goldstein et al., 2001; Go et al., 2013). Behavioural risk factors include hormone replacement therapy, oral contraceptive use, drug and alcohol abuse, dietary intake (>2300mg/day of sodium, >4700mg/day of potassium), physical inactivity, obesity and cigarette smoking (Goldstein et al., 2001; Go et al., 2013).

2.3 Pathology of Stroke

When a particular region of the brain suffers inadequate blood supply for longer than ten minutes, it is likely that some permanent cell death will occur (Blumenfeld, 2002). Neuron death as a result of prolonged and severe ischemia is called an infarct, also commonly known as a stroke (Kandel, Schwartz, Jessel, Siegelbaum, & Hudspeth, 2013). A stroke can generally be classified into two types, hemorrhagic and ischemic (Blumenfeld, 2002). Hemorrhagic strokes make up approximately 13% while ischemic strokes make up approximately 87% of all strokes (Roger et al., 2012). A hemorrhagic stroke occurs when a vessel bleeds out (Kandel et al., 2013). An ischemic stroke occurs when blood supply to a particular region of the brain is insufficient, usually due to an embolus or thrombus blocking a blood vessel (Blumenfeld, 2002).

2.4 Impairment Post-Stroke

Brain damage may occur in a variety of brain regions with varying severity; therefore, the effects of stroke on the body can be quite diverse. The location of brain damage depends on the artery affected (Purves et al., 2013). The severity of brain damage depends on whether other arteries were able to supply that location with any blood during the stroke and how quickly

medical treatment was received (Purves et al., 2013). The National Institute of Neurological Disorders and Stroke (NINDS) (2008) have broadly classified impairment after stroke in to five categories. These five categories include 1) Paralysis and problems with motor control, 2) Sensory disturbances, 3) Aphasia, 4) Problems with thinking and memory and, 5) Emotional disturbances. Further discussion will detail physical impairment (paralysis and problems with motor control) and cognitive impairment (problems with thinking and memory) that are common with stroke and are relevant to exercise in stroke survivors; the focus of this study.

2.4.1 Physical Impairment

A multitude of impairments of varying severity can affect a stroke survivor's ability to move. Only 14% of stroke survivors regain full physical function (Gordon et al., 2004), while 25 to 50% of survivors require some form of assistance with activities of daily living (Duncan et al., 2005; Gordon et al., 2004). The remaining 50% of survivors experience long term debilitating effects such as paresis (weakness) or paralysis (Duncan et al., 2005; Gordon et al., 2004). A few physical impairments which have the potential to limit purposeful exercise are further discussed.

Common physical impairments that may limit one's ability to exercise post-stroke include paralysis, paresis, spasticity and ataxia. Paralysis involves loss of function and paresis involves weakness; both of which generally affect the contralesional side of the body (NINDS, 2011). Hemiparesis has been found to occur in 50% of ischemic stroke survivors 65 years of age or older (Go et al., 2013). Spasticity is a hyperactivity of muscle tone and it can cause pain and hinder joint function (Duncan et al., 2005). This results in lack of movement at the joint which causes stiffening of surrounding tendons and ligaments (NINDS, 2011). Shoulder pain is a common side effect of spasticity, which occurs among stroke survivors due to lack of movement on the hemiparetic side (Duncan et al., 2005). Lastly, ataxia often occurs when the cerebellum

has been damaged and it involves difficulty coordinating movement, especially the maintenance of balance and posture (NINDS, 2011).

Any one impairment or combination of impairments can limit one's ability for movement and therefore, exercise and activities of daily living (ADLs). More specifically, these deficits can greatly reduce the mechanical efficiency of walking and thus increase the energy cost of walking compared to healthy controls (Olney, Griffin, Monga, & McBride, 1991; Waters & Mulroy, 1999). In order to accommodate these potential impairments, a recumbent stepper will be used for exercise in this study. The recumbent stepper allows for the hemiparetic limb to be secured to the pedal if need be and does not require use of the upper body to support oneself. Spasticity at the shoulder and paresis of the upper limbs are therefore not limiting factors. The recumbent stepper also accommodates for various forms of ataxia. Posterior trunk support will help in cases of postural imbalances and coordination of arm and leg movement is not required. Despite the various impairments that can exist in persons living with chronic stroke, the recumbent stepper can accommodate for many physical deficits, thus allowing for a greater portion of stroke survivors to participate in purposeful exercise.

2.4.2 Cognitive Impairment

In addition to physical impairments, cognitive function is also frequently impaired after stroke (Lesniak, Bak, Czepiel, Seniow, & Czlonkowska, 2008). Cognitive function reflects a set of processes that allow for the perception of a stimulus and the extraction of information in order to guide thoughts and actions to ultimately achieve a desired goal (Purves et al., 2013). Cognitive impairments after stroke can occur in isolation or concomitantly with physical impairments (Lesniak et al., 2008). Estimates of the prevalence of cognitive impairment after stroke range from 11.6 to 56.3% (Patel et al., 2002).

Cognitive impairment after stroke can be associated with a variety of negative consequences. Cognitive impairment can make it difficult for the stroke survivor to follow treatment guidelines and can limit functional recovery (Cumming, Marshall, & Lazar, 2013). It is also independently associated with significantly greater functional impairment, and affects one's ability to perform even basic ADLs and to live independently (Gordon et al., 2004; Tatemichi et al., 1994). After hospital discharge, dependent living either in one's own home or in a nursing facility was more likely in persons with cognitive impairment (55%) versus without cognitive impairment (33%) (Tatemichi et al., 1994). Cognitive impairment after stroke is also associated with greater rates of institutionalization (Pasquini, Leys, Rousseaux, Pasquier, & Henon, 2007), higher health care costs (Claesson, Linden, Skoog, & Blomstrand, 2005), a higher mortality rate (Patel et al., 2002) and a poorer quality of life (Hochstenbach et al., 2001).

Cognitive function is a multifaceted concept that can be classified into a variety of domains which include attention, executive function, visuospatial ability, memory and language (Cumming et al., 2013). Although the domains most commonly affected by stroke are not entirely clear, it is generally agreed that executive function and attention are two domains frequently impaired among stroke survivors (Ballard et al. 2003; Cumming, Tyedin, Churilov, Morris, & Bernhardt, 2012; Lesniak et al., 2008; Nys et al., 2005; Sachdev et al., 2004). Two studies reported that executive function and attention were the most frequently affected domains at 7 months (Nys et al., 2005) and 1 year (Lesniak et al., 2008) post-stroke. Additionally, executive function of post-stroke patients was independently correlated with the level of participation in rehabilitation (Skidmore et al., 2010). It is therefore not surprising that deficits in executive function during acute stroke were also the most significant predictor of functional impairment one year later (Lesniak et al., 2008).

Executive function refers to the cognitive processes that afford decision making, action planning and ultimately behaviour (Purves et al., 2013). More specifically, executive function refers to subcomponents of cognitively effortful processes such as the organization of action, mental flexibility, error monitoring, response selection, inhibition and working memory (Norman & Shallice, 1986; Purves et al., 2013). The focus of this study is to determine the effects of exercise on inhibition, a component of executive function. Inhibition involves the suppression of stimuli not relevant to behaviour (Purves et al., 2013). Control of executive functioning is exerted by a higher attentional system and thus, tasks measuring inhibition are also considered to be measurements of attention (Norman & Shallice, 1986). As detailed below, this thesis will examine whether a single session of aerobic exercise improves cognitive function, specifically the inhibitory component of executive function.

2.5 Stroke Rehabilitation

The primary goal of stroke rehabilitation is to regain functional independence and to optimize quality of life (HSF, 2009; NINDS, 2011). Rehabilitation begins once the individual has been stabilized in acute hospital care (NINDS, 2011; Duncan et al., 2005). This can occur within 24 to 48 hours post-stroke (NINDS, 2011). During this acute phase, priorities are to prevent recurrent stroke and complications, to manage general health and to mobilize (Duncan et al., 2005). Further medical stability allows for the focus of therapy to change to the assessment and recovery of physical and cognitive disabilities (Duncan et al., 2005). Both inpatient and outpatient rehabilitation units provide a multitude of medical services and access to a variety of rehabilitation specialists including physiotherapists, occupational therapists and recreational therapists (NINDS, 2011). Additional mediums include rehabilitation at patients' homes or at nursing homes.

Traditional post-stroke rehabilitation is critical for one's return to physical and mental health, attainment of independence and overall quality of life. Literature detailing the components of traditional stroke rehabilitation practices is limited and the inclusion of purposeful aerobic exercise during rehabilitation appears inconsistent. Recent evidence however, suggests that the incorporation of aerobic exercise may help improve physical as well as cognitive impairments after stroke.

2.5.1 Physical Rehabilitation

The aim of traditional post-stroke rehabilitation is to relearn lost skills as well as to acquire new ways of completing tasks (compensation) where necessary (NINDS, 2011). Recovery of mobility is an important aspect of physical rehabilitation and walking is often the end goal of mobility recovery (NINDS, 2011). Recovery of mobility can begin with stretching and range of motion exercises and advance to the rehearsal of isolated movements in order to achieve more complex movements such as walking (Duncan et al., 2005; NINDS, 2011). An important element of physical rehabilitation is the repetition of movement and practice of relearned skills (NINDS, 2011). Two potential additions to traditional post-stroke physical rehabilitation include functional electrical stimulation and constraint-induced movement therapy. Previous literature indicates functional electrical stimulation increases motor control and motor strength but it remains unclear as to whether there are improvements in long-term muscle function (Glanz, Klawansky, Stason, Berkey, & Chalmers, 1996). Constraint induced movement therapy forces use of the affected limb while discouraging use of the unaffected limb and may help recover upper extremity function (Duncan et al., 2005). One other technique requiring greater research is aerobic exercise and the potential for it to be incorporated into common practice to enhance the rehabilitation outcome of stroke survivors.

2.5.2 Cognitive Rehabilitation

Cognitive rehabilitation after stroke receives relatively little attention compared to physical rehabilitation. Speech language pathologists help those with aphasia (difficulty speaking, reading, writing or understanding speech) to improve comprehension and production of speech or develop alternative methods of communication (NINDS, 2011; HSF, 2009). Occupational therapists help stroke patients develop compensatory techniques so that functional tasks can be accomplished despite cognitive impairment (NINDS, 2011). Unfortunately, current cognitive rehabilitation strategies are limited and training techniques to improve attention and executive function, two cognitive domains frequently affected by stroke (Cumming et al., 2012; Sachdev et al., 2004; Ballard et al., 2003), do not appear to be incorporated into traditional rehabilitation settings. Aerobic exercise is one potential technique to incorporate into traditional stroke rehabilitation to improve cognitive as well as physical function, but further research is required.

2.6 Aerobic Exercise in Stroke Rehabilitation

Aerobic exercise is increasingly being recognized as an important component of stroke recovery. The American College of Sports Medicine (2000) defines aerobic exercise as the "use of large muscle groups for extended periods of time in activities that are rhythmic in nature, including but not limited to walking, stepping, running, swimming, cycling and rowing". Aerobic exercise may improve functional recovery and reduce secondary stroke risk (Pang, Eng, Dawson, & Gylfadottir, 2006). Emerging literature also suggests that it may contribute to cognitive or brain recovery.

Aerobic exercise is associated with increased aerobic capacity. Aerobic capacity is often compromised in the acute stroke population and may be as low as 50 to 70% of age and sex-matched sedentary controls (Eng, Dawson, & Chu, 2004; MacKay-Lyons & Makrides, 2004; Pang et al., 2006). This is due to a combination of low pre-stroke fitness and detraining due to sedentary behaviour post-stroke (Gordon et al., 2004; MacKay-Lyons & Makrides, 2004).

Low aerobic capacity has consequences for recovery. Low aerobic capacity is associated with increased risk of cardiovascular disease, including recurrent stroke, and it may also limit daily functions and independence (Gordon et al., 2004; Pang et al., 2006). An individual with low aerobic capacity has to work at a higher relative intensity compared to a fit individual in order to carry-out the same daily activities (Jeng, Chang, Wai, & Chou, 2003). Cress and Meyer (2003) suggest that there is a threshold of aerobic capacity needed to live independently and many stroke survivors do not meet this threshold (Eng et al., 2004; MacKay-Lyons & Makrides, 2002, 2004). Therefore, a low aerobic capacity after stroke may increase one's risk of cardiovascular disease and limit one's capacity for basic ADLs and overall independence.

Recent evidence suggests that the incorporation of aerobic exercise into stroke rehabilitation can improve physical aspects of stroke recovery. A systematic review completed by Pang et al. (2006) found that aerobic training (20-40 minutes, 3-5 days a week at 50-80% heart rate reserve) significantly improved aerobic capacity in stroke survivors. The review included studies of stroke survivors in acute and chronic stages of rehabilitation and aerobic exercise interventions such as walking, water-based aerobic training or cycling (Pang et al., 2006). Pang et al. (2006) also found a small but significant positive effect for better walking endurance and walking velocity with aerobic exercise, though it is unknown as to whether the improvement in walking was due to an increase in aerobic capacity and/or repeated gait practice.

In addition to improved aerobic capacity, Studenski et al. (2005) found that a combined strengthening and aerobic exercise program accelerated gains in daily functions; including endurance, balance and mobility relative to traditional rehabilitation. The exercise group also experienced greater gains in strength and community ambulation and had more persons who became independent in self-care compared to traditional rehabilitation (Studenski et al., 2005).

In addition to physical benefits, recent research also suggests that aerobic exercise may improve cognitive function in stroke survivors. Quaney et al. (2009) examined the effects of an 8 week aerobic training program (3 times per week, 45 minutes per session at 70% of maximal heart rate) on cognitive function. The aerobic group had significantly improved performance on a serial reaction time task and a predicted grip force modulation task which measured the ability for conditional learning. These positive results suggest aerobic exercise training can improve reaction time and motor learning in patients post-stroke (Quaney et al., 2009). Cognitive tests measuring executive function such as the Wisconsin Card Sorting Task, the Stroop Task and the Trail-Making Task A&B were also conducted; however, these tasks did not significantly improve after aerobic exercise (Quaney et al. 2009). The investigators suggested two reasons for the lack of significant differences. First, the small sample size used may have lacked the power to demonstrate change. Second, the tests of executive function may have lacked the sensitivity required to detect change (Quaney et al., 2009).

Another study by Kluding, Tseng and Billinger (2011) measured changes in executive function in individuals with chronic stroke after a 12 week training program. A typical session included aerobic exercise on a recumbent stepper for 20 minutes at 50% of maximal VO_2 and lower body strengthening exercises. Sessions took 60 minutes and were completed three times per week. After the 12 week period, working memory, as measured by backward digit span,

significantly improved and there was a trend for improvement in Flanker test accuracy scores that did not reach statistical significance. There was also a significant relationship between improved aerobic fitness and magnitude of improvement for the accuracy of incongruent Flanker trials. Findings by Kluding et al. (2011) suggest that the combination of aerobic and strengthening exercises in a training program may improve various measures of executive function in people with chronic stroke.

Ploughman and colleagues (2008) investigated whether a single treadmill exercise session improved cognitive function and an upper-extremity task in persons with chronic stroke. The exercise session was 20 minutes in duration and was completed at 70% of estimated heart rate reserve (HRR) or level 13 on the Borg Rating of Perceived Exertion (RPE) 6-20 scale (Appendix E). The cognitive tasks measured executive function, attention and processing speed. The Action Research Am Test (ARAT) was used to evaluate one's ability to grasp different sized blocks and cylinders and then release them. In this study, the exercise group had significantly improved performance on the ARAT but not on measures of cognitive function (Ploughman et al., 2008). Ploughman et al. (2008) suggested that the 20 minute treadmill intervention at a moderate intensity may not have been the right duration or intensity in order to elicit cognitive effects. The investigators recommend that future research be conducted in persons with brain injury to determine the exercise threshold required to induce cognitive effects (Ploughman et al., 2008). Results from healthy individuals suggest that both a single bout of aerobic exercise as well as greater aerobic fitness may improve cognitive function in young and older adults which will be further discussed in section 2.7. More sensitive measures or alternative intensities of exercise may exhibit similar changes among stroke survivors.

2.7 Aerobic Exercise and Cognitive Function in Healthy Adults

2.7.1 Single Session of Aerobic Exercise and Cognitive Function in Healthy Adults

Few studies have examined the effects of aerobic exercise on cognitive function in stroke; however there is evidence to suggest that a single session (bout) of aerobic exercise can enhance cognitive function in both young and older healthy adults. Both a meta-analysis by Chang and colleagues (2012) and another by Lambourne and Tomporowski (2010) found that one bout of aerobic exercise had acute positive effects on cognitive function in young healthy adults. Several potential effect modifiers and interactions were identified.

Firstly, exercise intensity was identified as one potential effect modifier. Chang et al. (2012) concluded that light and moderate intensities produced significant positive effects on cognitive function immediately after exercise while hard intensity had no effect. In contrast, when cognitive testing was delayed, light intensity exercise had a negative effect on cognitive function, but all other intensities produced significant positive effects (Chang et al., 2012). Conversely, Lambourne and Tomporowski (2010) found positive effects on cognition regardless of the exercise intensity; however they did not consider the time that cognitive measurements were taken post-exercise. Chang et al. (2012) also found that the timing of the cognitive task affected cognitive function (as seen above), independent of intensity. When combining the effects on cognitive function immediately and following a delay after exercise, negative effects were found when tests were administered between 0 and 10 minutes after exercise, significant positive effects were found between 11 and 20 minutes post-exercise and smaller, yet significant positive effects were also found after a 20 minute delay (Chang et al., 2012). A third potential modifier was exercise duration. Only exercise longer than 11 minutes in duration was found to be associated with positive cognitive effects (Chang et al., 2012).

Another moderator of the effects of exercise on cognitive function was task type. Tasks measuring executive function were found to produce significant effects immediately and following a delay after exercise while attention only improved immediately after exercise (Chang et al., 2012). It was also suggested that larger cognitive effects occur after cycling exercise than running exercise, though the reason for this is unknown (Lambourne & Tomporowski, 2010).

2.7.2 Aerobic Exercise and Executive Function in Healthy Adults

Executive function performance can be characterized using both behavioural performance measures and cortical processing measures. Measures of behavioural performance may include accuracy or error rate and reaction or response time. Response time refers to the total time for the task and can be defined as the time it takes for stimulus evaluation, response selection and response execution (Doucet & Stelmack, 1999). Cortical processing can be indicated by modulation of event-related potentials (ERPs), as measured with electroencephalography (EEG). An ERP is an electrical potential produced in the brain in response to a stimulus that is recorded at the level of the scalp via EEG (Picton, Lins, & Scherg, 1995). ERPs may be used in conjunction with cognitive tasks to quantify the effects of aerobic exercise on cortical processing.

The most commonly characterized ERP waveform examined relative to exercise is the P300. The P300 is a positive waveform occurring approximately 300 to 700 milliseconds after the onset of a stimulus and is thought to represent the updating of memory after sensory information has been analyzed (Donchin, 1981). The amplitude of the P300 is thought to reflect the amount of attentional resources used for a particular task (Kramer & Strayer, 1988; Wickens, Kramer, Vanasse & Donchin, 1983); the latency of the P300 is believed to indicate the time it takes to evaluate a stimulus (Kutas, McCarthy & Donchin, 1977). More specifically, the P300

results from the summation of inhibitory and excitatory postsynaptic potentials (Nieuwenhuis, Aston-Jones & Cohen, 2005). The P300 has been commonly used and assessed in conjunction with the Eriksen Flanker task to quantify the effects of exercise on executive function (Hillman, Snook, & Jerome, 2003; Hillman et al., 2004; Kamijo et al., 2007, 2009). The region of the brain believed to largely contribute to processes of executive function is the frontal cortex, specifically the dorsolateral prefrontal cortex (Kandel et al., 2013; Purves et al., 2013).

2.7.3 Single Session of Aerobic Exercise and Inhibition

The Eriksen Flanker task is commonly used to quantify the effect of both aerobic fitness and a single session of aerobic exercise on the inhibitory component of executive function (Hillman et al., 2003, 2004; Kamijo et al., 2007, 2009). The Eriksen Flanker task requires one to distinguish and respond to a central target stimulus while ignoring distractors found on either side (Colcombe & Kramer, 2003). Behavioural performance measures include accuracy and response time for congruent (target stimulus and distractors indicate same response) and incongruent (distractors indicate opposite response to target stimulus) conditions. Cortical processing is frequently characterized through the P300 waveform (amplitude and latency) elicited by the Eriksen Flanker task.

Both Kamijo et al. (2007) and Hillman et al. (2003) found that the P300 latency was significantly shorter during congruent trials than during incongruent trials at baseline. After a 20 minute cycling exercise session however, the congruent trial was no longer shorter than the incongruent trial, suggesting that exercise may have preferentially improved (shortened) the latency of the incongruent condition. This further suggests that tasks requiring greater effort (incongruent condition of Eriksen Flanker task) may be more sensitive to the effect of one bout of aerobic exercise and that perhaps exercise has a preferential effect on the prefrontal cortex

(Kamijo et al., 2007; Hillman et al., 2003). In addition, Kamijo et al. (2007; 2009) found that response time (the total time for the task) was significantly shorter after one bout of aerobic exercise. The positive effect on Flanker response time and P300 latency seems to be elicited by both light (30% VO_2 max) and moderate (50% VO_2 max) intensity exercise in both young and older individuals (Kamijo et al. 2009). This suggests that the effect of a single session of aerobic exercise on processing speed (latency) and overall response time is similar across the lifespan. Using a simpler Go/No-Go task, response time performance and P300 latency were unaffected by exercise (Kamijo et al. 2004). The authors suggested that the Go/No-Go Task (response inhibition) may require insufficient executive control to be sensitive to the effects of exercise (Kamijo et al. 2004).

The amplitude of the P300 has also been shown to be significantly improved (increased) after a single session of aerobic exercise (Kamijo et al., 2004, 2007, 2009; Hillman et al., 2003). Both light (RPE 7-9) and moderate (RPE 12-14) intensity exercise elicited a significantly larger increase in P300 amplitude than high intensity exercise (Kamijo et al. 2004, 2007). Unlike response time and latency however, P300 amplitude has only been shown to increase after a single session of aerobic exercise in younger adults and not in older adults (Kamijo et al. 2009).

Kamijo et al. (2009) suggested that an increase in P300 amplitude was not found in older adults due to a lower level of decision confidence. It is believed that more difficult tasks are associated with decreased levels of decision confidence, which results in smaller P300 amplitudes (Palmer, Nasman, & Wilson, 1994). It may be that older adults had such low decision confidence during the incongruent condition that any exercise effects were masked by very low P300 amplitude during the incongruent condition (Kamijo et al., 2009). Therefore, evidence suggests both light and moderate intensity aerobic exercise can increase the amount of

attentional resources devoted to a task, however the effects of aerobic exercise on P300 amplitude appear inconsistent across the lifespan.

In conclusion, at least a 20 minute bout of light and moderate intensity aerobic exercise appears to positively affect cognition, specifically the inhibitory component of executive function. Both response time and P300 latency significantly decrease after one bout of cycling in both young and older healthy adults. The amplitude of the P300 significantly increases after one bout of cycling; however, this effect only appears to occur in younger adults. The inconsistent impacts of exercise on the P300 amplitude between young and older adults suggest the potential for greater variability in other populations such as stroke survivors. Furthermore, after a single session of aerobic exercise, response time, P300 latency and P300 amplitude may be influenced by the difficulty level (amount of inhibitory control) of the task. Tasks which are more challenging (such as the incongruent condition of the Eriksen Flanker task) may be more sensitive to the effects of exercise.

2.7.4 Aerobic Fitness and Inhibition

In addition to the positive effects of a single session of aerobic exercise on cognitive function in healthy young and older adults, higher aerobic fitness is also associated with better cognitive function, specifically executive function. Research studies have found that both behavioural measures (response time and accuracy) as well as cortical measures from EEG recordings (P300 amplitude and latency) are enhanced in more aerobically fit and more physically active individuals. Of note, physically active individuals are typically more aerobically fit compared to less active individuals.

Hillman et al., (2006) found a positive association between physical activity levels and behavioural measures of performance (response time and accuracy) during a modified Eriksen

Flanker task. Higher physical activity level was associated with significantly decreased reaction time in both young and older adults. Accuracy was also significantly better but only among older adults (Hillman et al., 2006). Similar to one bout of aerobic exercise, the association between increased physical activity level and performance was also greater during the incongruent condition of a modified Eriksen Flanker task, which required a greater amount of inhibitory control, than during the congruent condition (Hillman et al., 2006).

Both Polich and Lardon (1997) and Hillman et al. (2004) found P300 amplitude during executive control tasks to be larger in individuals who participated in more physical activity each week and who therefore likely had greater aerobic fitness. Polich and Lardon (1997) found that during visual and auditory oddball tasks, young adults in a high exercise group had larger P300 amplitudes versus a low exercise group (Polich & Lardon 1977). Young adults in the high exercise group also had a trend towards shorter P300 latency in comparison to the low exercise group (Polich & Lardon, 1997). Hillman et al., (2004) found that during a modified Eriksen Flanker task, moderate and highly active older adults demonstrated larger P300 amplitude versus a group of young healthy controls who were not classified by activity level (Hillman et al., 2004). Highly active older adults also demonstrated shorter P300 latency times in comparison to low and moderately active older adults and similar P300 latency times in comparison to the younger controls (Hillman et al., 2004).

In conclusion, physical activity appears to be positively associated with the inhibitory component of executive function. Cortical measures of the P300 reveal shorter latency and larger amplitude during auditory and visual oddball tasks as well as during a modified Eriksen Flanker task in higher versus lesser fit individuals (Hillman et al., 2004; Polich & Lardon, 1997). Behavioural measures reveal faster reaction times and better accuracy in high versus less active

individuals (Hillman et al., 2006). Positive associations between physical activity and reaction time and P300 amplitude appear consistent across the lifespan whereas associations with accuracy and P300 latency only appear to be greater among older adults.

2.8 Potential Mechanisms

There are several potential mechanisms responsible for the positive effects of aerobic exercise on cognitive function, including increased cerebral blood volume (Pereira et al., 2007) and increased levels of brain-derived neurotrophic factor (BDNF) (Huang, Larsen, Ried-Larsen, Moller & Andersen, 2014). Increased cerebral blood volume may contribute to both angiogenesis (Kleim, Cooper & Vandenberg, 2002) and neurogenesis (Pereira et al., 2007). Increased levels of BDNF may induce neuronal synthesis and development as well as increases in long-term potentiation (for review, See Huang et al., 2014).

More relevant to the current study, hypotheses to explain the beneficial effects of a single session of aerobic exercise on cognitive (executive) function include: 1) Increases in cerebral blood flow (Smith, Paulson, Cok, Veber & Tian, 2010; Marmeleira, 2013); 2) Increases in BDNF concentrations in the brain (Levine, Dreyfus, Black & Plummer, 1995; Jovanovic, Czernik, Fienberg, Greengard & Sihra, 2000) and 3) Increases in both peripheral and central catecholamine concentrations (McMorris, Collard, Corbett, Dicks & Swain, 2008; Meeusen et al., 1997; Peyrin, Pequignot, Lacour & Fourcade, 1987). The three potential mechanisms to improve cognitive function after one bout of aerobic exercise are described below.

2.8.1 Increased Cerebral Blood Flow

Increased cerebral blood flow may contribute to enhancements in cognitive functioning after a single session of aerobic exercise; however results regarding the location of brain blood

flow are somewhat inconsistent. Smith et al., (2010) found that global cerebral blood flow was significantly elevated at 30 minutes after the completion of 30 minutes of moderate intensity cycling exercise. In contrast, MacIntosh et al., (2014) found no significant increase in global cerebral blood flow but found significantly increased cerebral blood flow in the cerebral white matter at 10 and 40 minutes post-exercise. It seems reasonable that increased cerebral blood flow could increase the availability of resources either as a result of or resulting in increased metabolism in the brain; thereby improving cognitive function. However, there is minimal evidence to date to support acute increases in cerebral blood flow as a mechanism to link exercise and enhanced cognitive performance.

2.8.2 Increased BDNF Concentrations

It is well established that BDNF plays an important role in neuronal synthesis and that BDNF concentrations are elevated after chronic exercise (for review, see Huang, Larsen, Ried-Larsen, Moller & Andersen, 2014; Schinder & Poo 2000). BDNF may also play an acute role in the enhancement of cognitive function via improved synaptic transmission after a single bout of aerobic exercise. A review by Huang et al., (2014) concluded that there were increased peripheral concentrations of BDNF in healthy humans during and immediately after one bout of aerobic exercise. Additional literature from animal models have found central increases in BDNF protein and mRNA expression in the rat hippocampus (Huang et al., 2006; Soya et al., 2007) and cortex (Rasmussen et al., 2009) after a delay post-exercise (single session of treadmill running). Of note, the exercise intensity which elicited the greatest increase in BDNF was varied across animal studies.

Increased BDNF concentrations in the brain may contribute to improved cognition by several mechanisms. Increased BDNF concentrations increase the amplitude and firing rate of

excitatory postsynaptic potentials in rats (Levine et al., 1995). Increased postsynaptic excitation is thought to be, at least partially, the result of heightened responsiveness on the postsynaptic cell via a phosphorylation pathway (Levine et al., 1995). Greater postsynaptic charge then provides the opportunity for increased frequency of excitatory postsynaptic potentials (Levine et al., 1995). BDNF also indirectly influences synaptic transmission by binding to a kinase receptor (Jovanovic et al., 2000). This binding subsequently activates downstream signaling processes that results in increased glutamate (GLU) release (Jovanovic et al., 2000). GLU is a brain neurotransmitter involved in synaptic transmission and increased GLU levels can also result in greater excitatory postsynaptic potentials.

Interestingly, the increased plasma BDNF concentrations in healthy humans post-exercise occurred immediately after exercise cessation and returned to basal levels during recovery from exercise (Huang et al., 2014). Specifically, effects lasted less than 30 minutes (Huang et al., 2014). In contrast, central levels of BDNF protein and mRNA expression in rats were not significantly elevated from pre-exercise levels until two or more hours after exercise cessation (Huang et al., 2006; Rasmussen et al., 2009; Soya et al., 2007). Therefore, if BDNF is responsible for improvements in cognitive function after exercise, the duration of the effects is likely to be very short or much delayed.

2.8.3 Increased Brain Neurotransmitter Concentrations

A rise in central neurotransmitters (primarily catecholamines) may be responsible for the link between exercise and improved cognitive function. Studies with animals measure neurotransmitter levels in the brain after exercise while studies with humans often use peripheral measures of catecholamines as a proxy for brain neurotransmitter levels. These brain neurotransmitters include norepinephrine (NE), dopamine (DA) and glutamate (GLU) (Meeusen

et al., 1997). Of note, the practice of using peripheral measures as a proxy is not supported by all, since catecholamines do not cross the blood-brain barrier.

Levels of brain neurotransmitters are enhanced for a prolonged period post-exercise, though evidence primarily arises from animal models. Increased concentrations of NE have been observed after one bout of moderate intensity aerobic exercise in both the rat frontal cortex and rat striatum (Meeusen et al., 1997; Pagliari & Peyrin, 1995). Levels remained significantly elevated from baseline until 20 to 120 minutes post-exercise, depending on exercise duration. Specifically, Pagliari & Peyrin (1995) found that the duration of NE elevation was proportional to the exercise duration. Increased concentrations of DA were also observed in the rat striatum and the rat hippocampus from 40 minutes to 120 minutes post exercise (Goekint et al., 2012; Meeusen et al., 1997). Finally, increased concentrations of glutamate (GLU) have been observed in the rat striatum for up to 40 minutes after a single session of treadmill running (Meeusen et al., 1997). In humans, Galbo, Holst and Christensen (1975) found peripheral catecholamine levels had returned to baseline by 30 minutes after the termination of exercise; however, it is possible that the difference in duration is due to the location of measure (peripheral versus central) and that central measures, if possible, would show a prolonged effect in humans as well. This evidence suggests that there is an increase in brain neurotransmitter concentrations after a single session of aerobic exercise, but also suggests that levels are elevated for a prolonged period of time after exercise.

Increased concentrations of brain neurotransmitters, such as those brought on by exercise, are thought to positively influence cognitive function due to enhanced synaptic transmission. Larger concentrations of neurotransmitters induce larger amplitude excitatory postsynaptic potentials (Nieuwenhuis, Aston-Jones & Cohen, 2005); such as those observed after exercise in

the P300. These enhancements in the amplitude of excitatory postsynaptic potentials are thought to represent improvements in cortical processing.

The neurotransmitter most commonly studied in conjunction with exercise and cognition is arguably NE. Pertinently, NE innervation is highest in the inferior parietal and frontal cortices (Nieuwenhuis et al., 2005). These areas are involved in memory and executive function respectively (Kandel et al., 2013; Purves et al., 2013). If NE were part of the mechanisms linking exercise and cognitive function, we would expect exercise to have preferential effects in these regions, which is the case.

There is strong evidence from animal models to suggest that brain neurotransmitters are increased after exercise and that the time course of effects is prolonged. In particular, the density of NE is highest in regions associated with memory and executive function, which are enhanced by exercise. It is likely that increases in neurotransmitters enhance synaptic transmission and therefore can positively influence cognitive function.

3.0 Study Rationale

Up to 57% of stroke survivors have some cognitive impairment (Patel et al., 2002), which can also contribute to functional impairments (Tatemichi et al., 1994). Thus, an investigation of modalities to improve cognitive recovery after stroke was warranted. Increasing evidence suggests cognitive function, especially executive function, may be enhanced after a single session of aerobic exercise. Despite the research in healthy young and older populations, few studies have investigated the effects of one bout of aerobic exercise in patient populations such as stroke survivors (Ploughman et al., 2008). It was hypothesized that aerobic exercise may enhance cognitive function, especially executive function, among stroke survivors. This study used a modified Eriksen Flanker task to characterize executive function. This task measures executive function and was used to test the inhibitory component of executive function among stroke survivors before and after a single session of aerobic exercise. This task has previously shown to be sensitive to the effect of exercise among healthy young (Hillman, 2003; Kamijo, 2007) and older (Kamijo, 2009) adults. We used EEG in conjunction with this task as a sensitive measure of changes in cortical processing; specifically, alterations in the amplitude and latency of the P300.

4.0 Objectives and Hypotheses

Objectives:

1. To examine the change in cortical processing among stroke survivors after a 20 minute bout of moderate intensity aerobic exercise in comparison to a rest condition during an executive function task: modified Eriksen Flanker task for inhibitory control.

2. To examine the change in behavioural performance among stroke survivors after a 20 minute bout of moderate intensity aerobic exercise in comparison to a rest condition during an executive function task: modified Eriksen Flanker task for inhibitory control.

3. To determine the duration of changes among stroke survivors in behavioural performance and cortical processing effects after a 20 minute bout of moderate intensity aerobic exercise.

Hypotheses:

1. After a 20 minute bout of moderate intensity aerobic exercise, cortical processing will be affected in the following manner: Improvements during the modified Eriksen Flanker task (inhibitory component of executive function) exhibited by decreased P300 latency but no change in P300 amplitude.
2. After a 20 minute bout of moderate intensity aerobic exercise, behavioural performance will be affected in the following manner: Change in the modified Eriksen Flanker task (inhibitory component of executive function) exhibited by decreased response time but no change in accuracy.
3. After a 20 minute bout of moderate intensity aerobic exercise, effects on behavioural performance and cortical processing will last up until and including 20 minutes post-exercise; after which effects will decrease and no longer by significantly different from baseline by 40 minutes post-exercise.

5.0 Methods

5.1 Ethics

This study has been reviewed and approved by the Office of Research Ethics at the University of Waterloo (ORE #17856). All participants voluntarily provided informed consent. Participants were aware of their rights to withdraw from this study at any time. All data collection took place at the University of Waterloo.

5.2 Participants

Participants were primarily recruited from the University of Waterloo Neurological Patients' Database (NPD). The NPD is made up of patients whom have previously agreed to provide their personal information in order to be contacted for participation in research studies. Of 485 patients in the NPD, 33 people were eligible for the study. Inclusion and exclusion criteria for this study are listed in Table 5.1. Suitable patients from the NPD were initially contacted by phone. At this time, a brief description of the study was provided. Interested participants were then sent a package containing Information/Consent Forms (Appendix A) as well as a PARmed-X form. A follow-up phone call ensured each individual's PARmed-X form had been signed by a physician, at which point the baseline session was scheduled. Of the 33 eligible participants, only 8 agreed to participate and had a physician approve them for suitable exercise. Explanations for non-participants are shown in Figure 5.1. One additional participant found out about the study and asked to be involved. Therefore 9 participants took part in this study.

Table 5.1: Stroke participant inclusion and exclusion criteria

Inclusion Criteria	Exclusion Criteria
· Age ≥ 18 years · Males and females · Ischemic and hemorrhagic stroke · Chronic stroke (≥ 6 months post-stroke) · Ability to provide own informed consent · Ability to exercise on the Nu Step recumbent stepper · Ability to understand process and instructions · Physician's Approval (PARmed-X)	· Uncontrolled diabetes (blood sugar not well regulated by medication, diet or exercise) · Uncontrolled hypertension (blood pressure not well regulated with or without medicine · Hospitalization for myocardial infarction, heart failure or heart surgery within the last 2 years · Unstable angina · Other cardiovascular morbidity which limits exercise tolerance (heart failure, complex arrhythmias, abnormal BP responses) · Resting systolic blood pressure >200mmHg and/or diastolic blood pressure > 110mmHg · Major neurological condition (Dementia, Epilepsy, Parkinson's) · Have chronic obstructive pulmonary disease · Have musculoskeletal impairments or pain limiting ability to use recumbent stepper · Global aphasia · Visual impairment that prevents viewing of computer screen · Allergies to electrode gel or adhesive

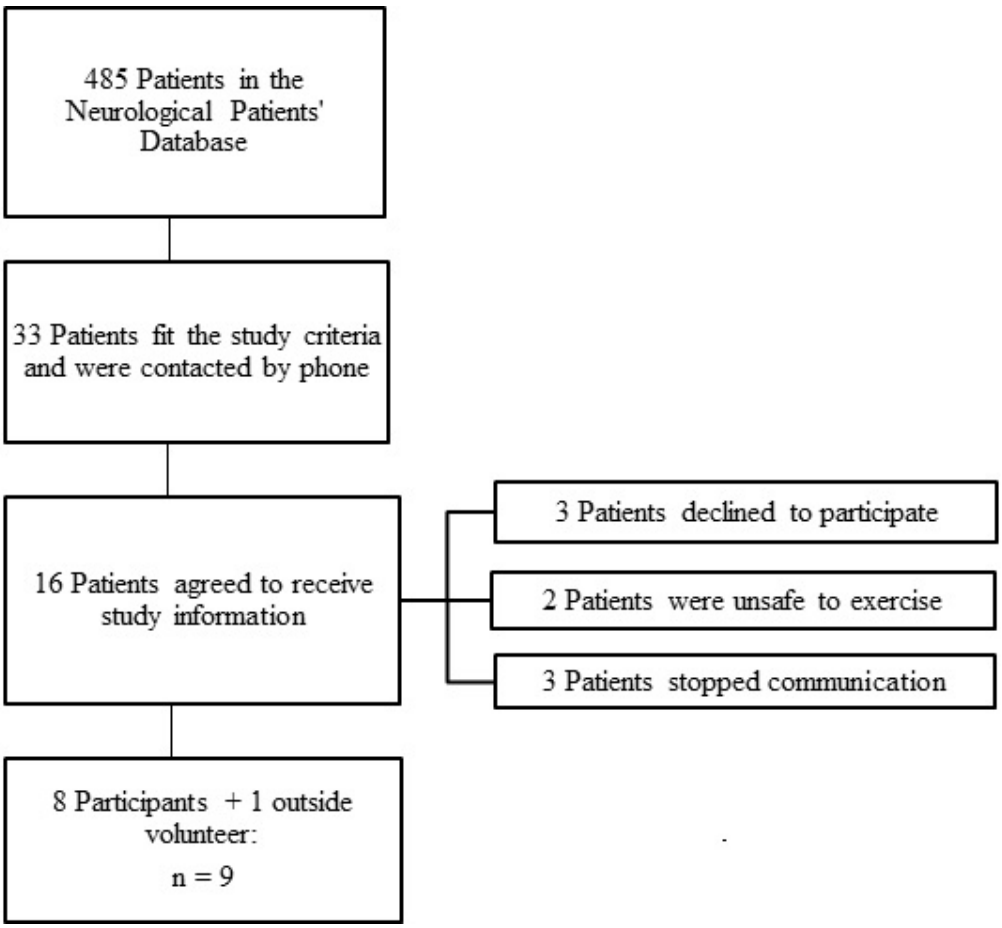

Figure 5.1: Flow of Participant Recruitment

5.3 Protocol Overview

This study used a repeated measures design. The study required three separate sessions in the laboratory with cognitive function compared across the latter two sessions. The first session was always a baseline session while the order of the following two sessions was randomized to minimize the potential for practice effects. The following two sessions consisted of a rest session and an exercise session. Participants could return to the lab for a second session three days after baseline completion; however rest and exercise sessions were separated by 2 to 3 weeks to minimize practice effects but maximize lifestyle consistency. Within each participant, rest and exercise sessions were completed at the same time of day to limit circadian rhythm effects. Participants were also asked to abstain from caffeinated beverages and purposeful exercise on all testing days.

For the baseline session, participants arrived to the lab with completed PARmed-X forms and a current list of medications. Participants first provided informed consent (Appendix A). They then completed the arm and leg components of the Chedoke-McMaster Stroke Assessment (CMSA) to assess baseline physical impairment (CMSA, 2008) and the Montreal Cognitive Assessment (MoCA) to assess baseline cognitive function (Nasreddine, 2013). These assessments can be found in Appendix B and Appendix C respectively. Additional measures included personal information and stroke characteristics (see section 5.5 for more detail). Finally, participants completed a submaximal exercise test on a recumbent stepper (detailed in section 5.4.1 and Appendix D). Participants were also given a minimum of 140 practice trials of the modified Eriksen Flanker task, suggested by McMorris et al. (2003) to be the minimum number of trials necessary to eliminate potential practice effects. Finally, participants were introduced to

the EEG equipment and the testing procedures for subsequent sessions. Participants were also given the opportunity to address any questions or concerns at this time.

During the rest session, participants returned to the laboratory, were given a review of procedures and were re-introduced to the cognitive test (the modified Eriksen Flanker task) with at least 30 practice trials. Participants then performed the cognitive task prior to and immediately, 20 minutes and 40 minutes after a 20 minute rest period. During the 20 minute rest, participants sat quietly on the recumbent stepper. A description of the modified Eriksen Flanker task can be found in section 5.5.2 and a schematic is included in Appendix F.

At the exercise session, participants returned to the laboratory, were given a review of procedures and were re-introduced to the cognitive test (the modified Eriksen Flanker task) with at least 30 practice trials. Participants then performed the modified Eriksen Flanker task prior to as well as immediately, 20 minutes, and 40 minutes after an aerobic exercise session. The exercise session involved 20 minutes on a recumbent stepper (Nu-Step T5 model) at a moderate intensity. The intensity/work rate corresponded with the level of resistance on the recumbent stepper that elicited 45-55% of the participant's heart rate reserve (HRR) during the submaximal exercise test (described in section 5.4.1). A HRR of 45-55% is considered by the American College of Sports Medicine to be a moderate intensity (ACSM, 2013). During the test, participants reported ratings of perceived exertion (RPE) every four minutes (Borg 6-20 scale, included in Appendix E). A RPE of 12-13 on the 6-20 scale is associated with moderate intensity exercise (ACSM, 2013). Heart rate (HR) and blood pressure (BP) were monitored throughout for safety. HR measures were taken with a heart rate monitor at rest and during each minute of exercise. BP measurements were taken with a blood pressure monitor at rest and a minimum of every four minutes during the exercise.

5.4 Exercise

A Canadian Society for Exercise Physiology – Certified Exercise Physiologist (CEP) was present for all submaximal exercise tests and exercise sessions. In addition to monitoring HR and BP, the CEP also conducted a 3-lead Electrocardiogram (ECG) to record electrical activity of the participant's heart. This allowed for the heart beat to be monitored.

5.4.1 Submaximal Exercise Test

Participants completed a submaximal exercise test on a recumbent stepper to assess individual responses to exercise and to determine the work rate for the exercise session. The submaximal protocol was modified from a maximal exercise test protocol designed for chronic stroke survivors on a recumbent stepper (Billinger, Tseng, & Kluding, 2008). The protocol included up to eight, 2 minute stages, each at a cadence of 80 steps per minute. The detailed protocol is provided in Appendix D. The test was terminated for any of the following reasons: 1) Participant reached 80% of age-predicted max heart rate (HRmax), adjusted for beta-blocker use if appropriate (Brawner et al., 2004); 2) Participant exceeded a systolic blood pressure > 250 mmHg and/or diastolic blood pressure > 110 (ACSM, 2013); 3) Participant experienced a drop in systolic blood pressure of >10mmHg despite an increase in workload (ACSM, 2013); 4) Participant was unable to maintain the stepping cadence; 5) Participant complained of chest pain; or 6) Participant reached volitional fatigue or requested to stop. BP was measured at rest and every four minutes during exercise (American Diagnostic Corporation, 1993). HR was also recorded at rest and every 30 seconds during exercise (Polar Electro FS1). These HR recordings were used to determine the level of resistance on the recumbent stepper that elicited an exercise response corresponding to 45-55% of the participant's HRR, the work rate for exercise sessions.

In addition, participants reported rating of perceived exertion (Borg 6-20 scale, included in Appendix E), at each stage of the protocol.

5.4.2 The Exercise Prescription

The percent heart rate reserve (HRR) method was used to determine the target HR for the exercise session. The intensity/work rate for the 20 minute exercise session corresponded with 45-55% of the participant's HRR, which is considered by the American College of Sports Medicine (2013) to be a moderate intensity. HRR is the difference between resting and maximal heart rate (ACSM, 2013). Resting HR was recorded at baseline and a predictive maximal HR was calculated via one of three formulas according to the participant's age and current medications. The formulas used to determine target heart rate are in Appendix H while a sample calculation of target HR can be found in Appendix I. The HR recordings were then examined to find the level on the recumbent stepper that elicited the target HR. The exercise session was completed at this level.

5.5 Measures

Basic personal information and stroke characteristics were recorded for each participant at baseline. Personal information included age, sex, height, weight, years of education, resting HR and resting BP. Stroke characteristics included the date , type (ischemic of hemorrhagic) and side of impairment. Stroke characteristics were obtained from the Neurological Patients' Database. A current list of medications was provided on the day of testing as well as information regarding handedness pre and post-stroke.

5.5.1 Physical Function

Chedoke-McMaster Stroke Assessment (CMSA)

Physical impairment of the arm and leg was assessed using the CMSA. The CMSA was created for the physical assessment of stroke survivors in a rehabilitation setting (CMSA, 2008). This took approximately 10 minutes to administer. Instructions for the arm and leg assessments of the CMSA can be found in Appendix B.

5.5.2 Cognitive Function

Montreal Cognitive Assessment

Global cognitive function was assessed using the MoCA. The MoCA is a simple, yet sensitive cognitive screening tool used to identify mild cognitive impairment (Nasreddine et al., 2005). The test took 10 minutes to administer and was used to assess a variety of cognitive domains including attention and concentration, executive function, memory, language, visuospatial ability, conceptual thinking, calculations and orientation (Nasreddine et al. 2005). The MoCA can be found in Appendix C.

Eriksen Flanker Task

A modified Eriksen Flanker task was used to assess the inhibitory component of executive function. It requires one to identify and respond to a central target stimulus, which is flanked by two distractors on either side (Colcombe & Kramer, 2003). In this study, the stimuli and distractors were black horizontal arrows displayed on a white background. Each arrow was 12cm in height and 13cm in width. The arrowheads were presented for 200ms with a 3000ms inter-trial interval. The participants sat at a distance of 200cm from the screen and had to respond to whether the central arrow was pointing in the left or right direction. A response was indicated

by clicking the left or right button on a small computer pad. The distractors pointed in the same (congruent) or opposite (incongruent) direction, which were randomized across 200 trials. Completion of 200 trials took approximately 11 minutes. Instructions directed the participant to respond as quickly and as accurately as possible. Behavioural measures during this task included overall response time and accuracy. Response time was recorded from the onset of the stimulus (arrow display) until a response had been indicated. A schematic of the modified Eriksen Flanker task is included in Appendix F.

5.5.3 Electroencephalography (EEG)

EEG was recorded during the cognitive tests in both the rest and exercise sessions. Event-related potentials (ERPs) linked to the cognitive stimuli during the modified Eriksen Flanker task were recorded and used to evaluate changes in cortical processing. Specifically, the amplitude and latency of the P300 waveform in response to the presented stimuli were evaluated as indicators of cortical processing associated with the cognitive task.

The EEG signal was measured using a *QuikCap* (Compumedics Neuroscan, Charlotte, NC). Electrodes used in this study included Fz, F3, F4, F5, F6, CZ, C3, C4, C5, C6, Pz, P3, P4, P5, P6 and Oz; as arranged in the International 10-20 system (see Appendix G for a diagram of the location of electrodes). Electrodes were used on the midline and on both the right and left sides as well as in the front, middle and back of the cap. Use of electrodes on both sides allowed for comparison of the lesional versus the contralesional side. Additional electrodes were placed on the participant's head, held in place by an adhesive ring. These electrodes were placed behind the left and right ears, to the left and right of the left and right eyes respectively and above and below the left eye. The mastoid electrodes acted as reference for the EEG signal and the

electrodes around the eyes monitored eye movements to allow for the removal of blink trials. Impedance of each electrode was less than 10 kΩ and EEG was recorded at 500Hz.

5.6 Analysis

5.6.1 Electroencephalography Recordings

Epochs for evaluation of the P300 during the modified Flanker were created 200ms prior to stimulus onset to 1000ms post-stimulus. Each epoch was baseline corrected to the 200ms pre-stimulus interval. The signal was filtered using a 0.5Hz low-cut off and a 30Hz high-cut off. Trials with response errors and eye blinks (rejection: ± 150μV) were excluded from analysis and the remaining trials were averaged. The P300 was defined as the most positive peak occurring 300 to 700ms after stimulus presentation (Kamijo et al., 2007, 2009). EEG recordings and processing were performed using Curry Neuroimaging Suite 7.0.7X and 7.0.7SB respectively.

5.6.2 Statistical Analysis

Analysis was performed using SAS 9.3. Analysis was conducted for both behavioural measures (response time and response accuracy) and EEG measures (P300 amplitude and P300 latency). Histogram and probability plots were generated and inspected for normality. After confirmation of normality, a repeated measures analysis of variance (ANOVA) was conducted with factors for session (exercise versus rest), time (pre, immediately post, 20 min post, 40 min post) and congruency (congruent versus incongruent). For EEG measures, additional factors for electrode site included side (lesional, contralesional or the Z-line/midline) and row (frontal, central, parietal). Post hoc analysis involved use of the Tukey Test to identify specific differences within the significant interactions. The significance level was set at $p < 0.05$.

6.0 Results

Nine participants, 6 males and 3 females, mean age of 57.8 ± 11.4 (43-71) completed this study. All participants had experienced a stroke within the last five and a half years. Additional participant characteristics are described in Table 6.1.

Table 6.1: Participant Characteristics (n=9)

Characteristic	Mean ± SD or n (%)
Age (years)	57.8 ± 11.4
Height (cm)	174.6 ± 8.3
Weight (kg)	78.3 ± 11.8
Years of Education	15.5 ± 3.4
CMSA (Score out of 7)	
Arm	5.3 ± 2.4
Leg	6.3 ± 1
MoCA (Score out of 30)	25.3 ± 4.9
IPAQ	
Low	3 (34%)
Moderate	5 (55%)
High	1 (11%)
Time Post-stroke (months)	37.6 ± 20
Stroke Type*	
Ischemic	6 (67%)
Hemorrhagic	0 (0%)
Both	1 (11%)
Stroke Side	
Left	2 (22%)
Right	7 (78%)
Handedness (Pre – Post)**	
Left – Left	0 (0%)
Left – Right	2 (22%)
Right – Right	6 (67%)
Right – Left	1 (11%)
Diabetes	0 (0%)
Hypertension	3 (33%)
High Cholesterol	5 (56%)

*Two participants did not report. **Handedness: Pre = before the stroke, Post = Preferred hand used for testing.
Note: One participant used the affected hand for testing.

6.1 Exercise Intensity

Table 6.2 displays the participant means for HRmax, HRrest, exercise session HR, recumbent stepper resistance level and RPE from the exercise session. All participants were able to maintain an average of 45-55% HRR within 5 beats per minute with the exception of two. These two participants however, as well as all other participants, rated the exercise intensity across the 20 minutes to be at an RPE of 11-14, which is approximately a moderate intensity level based on Borg's RPE 6-20 Scale (PAL, 2014).

Table 6.2: Exercise Session Characteristics (mean ± SD)

HRmax (bpm)	166 ± 7.3
HRrest (bpm)	74.3 ± 13.2
Exercise Session HR (bpm)	111.5 ± 13.3
Nu Step Resistance Level	5.4 ± 1.1
RPE	13.1 ± 1.0

6.2 P300 Amplitude (μV)

There were significant main effects for row [F (2, 16) =5.82, p=0.0126] and side [F (2, 16) =5.25, p=0.0177]. For row, amplitude was largest in the P row (mean ± SD: 9.70 ± 6.10) and smallest in the F row (6.10 ± 4.14). With respect to side, amplitude was largest in the Z-line (8.82 ± 5.83) and smallest on the contralesional side (6.90 ± 3.77). There was also a significant interaction for row×side [F (4, 32) =4.91, p=0.0033]. There was quite a lot of variability across electrode sites, however P300 amplitude was largest at the Pz electrode site (11.10 ± 6.50) and smallest at the F-contralesional electrode site (5.73 ± 3.53). Finally, there was a significant

interaction for session×time×row [F (6, 48) =3.16, p=0.0107]. Follow up analyses identified a significant session×time interaction across the F row only [F (3, 24) =3.93, p=0.0206], though the interaction neared significance across the P row [F (3, 24) =2.70, p=0.0679). Specifically, Tukey post hoc analyses indicated that P300 amplitude in the F row was significantly greater 40 minutes post-exercise in comparison to 40 minutes post-rest (p=0.0067). Figure 6.1 uses Fz as an example of the session×time interaction in the F row and Figure 6.2 displays the corresponding P300 waveform. No significant effect or interaction involving congruency was observed. Figure 6.3 displays the mean P300 amplitude at Fz for congruent and incongruent conditions by session and time.

6.3 P300 Latency (ms)

P300 latency analysis revealed a significant main effect for congruency [F (1, 8) =24.62, p=0.0011), such that the average latency was shorter during congruent trials (mean ± SD: 466.54 ± 80.43) than in the incongruent trials (489.09 ± 87.83). There was also a significant main effect for row [F (2, 16) =4.14 p=0.0356], such that the average latency was shortest in the P row (459.14 ± 76.66) and longest in the F row (500.81 ± 82.69). In addition, there was a significant 5-way interaction for session×time×congruency×row×side [F (12, 96) =1.92, p=0.0411]. Follow-up tests indicated a significant session×time interaction at the C lesional electrode site for both the congruent [F (3, 24) =3.95, p=0.0202] and incongruent [F (3, 24) =4.23, p=0.0155] stimuli. Tukey post hoc analysis indicated that P300 latency was significantly shorter 20 minutes post-exercise in comparison to 20 minutes post-rest across congruent (p=0.0187) and incongruent (p=0.0031) stimuli. Figure 6.4 displays this session×time interaction at the C lesional site across congruent and incongruent stimuli.

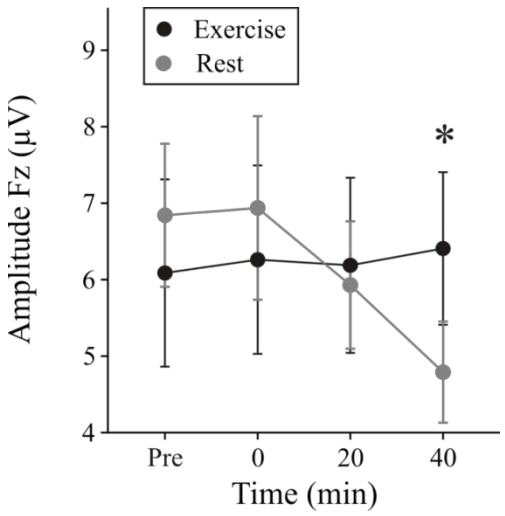

Figure 6.1: Mean P300 amplitude by session and time at the Fz site
* indicates significant difference between rest and exercise conditions $p<0.05$

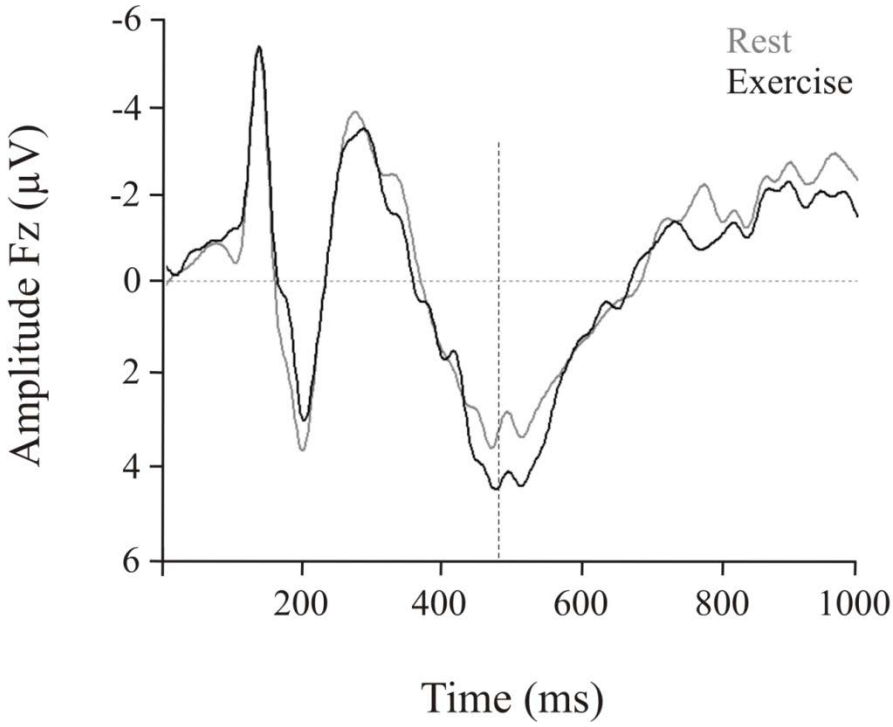

Figure 6.2: P300 tracing by session at 40 minutes post-intervention (across both congruency conditions). Fz is used to represent the significant difference across the F row

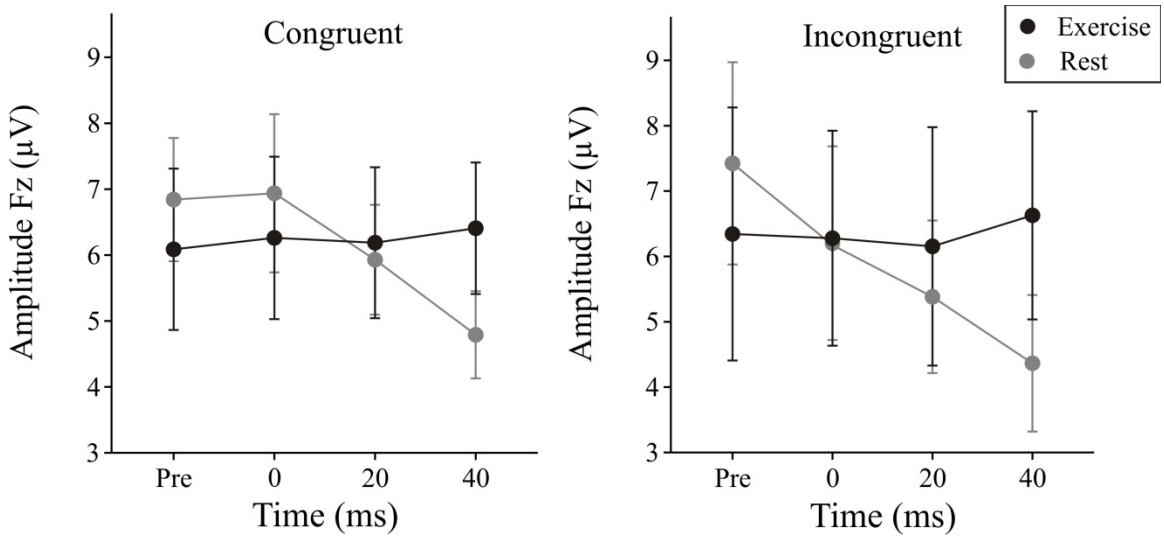

Figure 6.3: Mean P300 amplitude for congruent and incongruent conditions by session and time at the Fz site

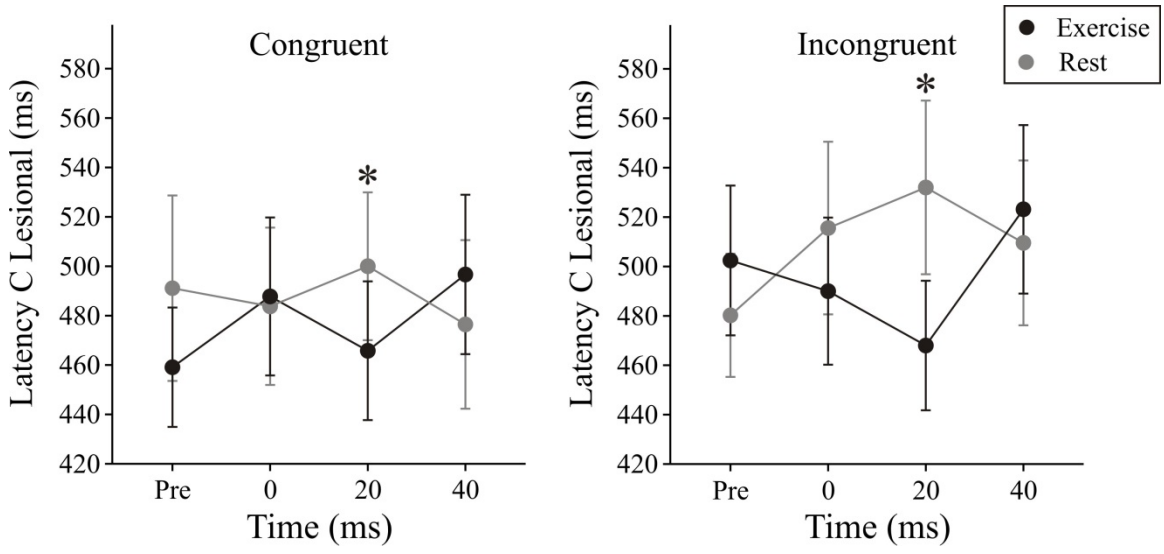

Figure 6.4: Mean P300 latency for congruent and incongruent conditions by session and time at the C Lesional site

* indicates significant difference between rest and exercise conditions $p<0.05$

6.4 Behavioural Measures

Analysis of response time (ms) revealed a main effect for congruency [F (1, 8) =75.54, p<0.0001] such that average response time was shorter for congruent stimuli (mean ± SD: 531.80 ± 87.42) compared to incongruent stimuli (590.73 ± 76.37). Analysis of accuracy (% correct) demonstrated a main effect for time [F (3, 24) =3.33, p=0.0365] in which the pre time point was significantly more accurate than both 20 minutes (p=0.0135) and 40 minutes (p=0.0316) post-intervention. In addition, immediately post-intervention (0 minutes) was more accurate than 20 minutes post-intervention (p=0.0491). Table 6.3 displays the group means and standard deviations for both response time and accuracy (% correct) during congruent and incongruent trials at each of the four time points in the rest and exercise sessions.

Table 6.3: Behavioural measures by session, time and congruency (mean ± SD)

		Accuracy (% correct)		**Response Time (ms)**	
		Congruent	Incongruent	Congruent	Incongruent
Pre	Rest	89.9 ± 14.4	85.2 ± 18.0	517.2 ± 63.6	578.5 ± 42.7
	Exercise	88.7 ± 16.0	86.7 ± 16.3	509.6 ± 59.4	594.6 ± 76.0
0	Rest	92.5 ± 13.1	77.3 ± 35.6	517.3 ± 81.1	578.8 ± 66.9
	Exercise	89.1 ± 14.0	86.1 ± 18.1	519.9 ± 83.8	578.9 ± 78.9
20	Rest	87.3 ± 15.9	75.2 ± 34.6	537.6 ± 93.0	595.7 ± 67.9
	Exercise	86.5 ± 12.9	76.5 ± 27.2	547.7 ± 102.2	620.7 ± 113.9
40	Rest	88.8 ± 14.3	75.4 ± 34.7	540.9 ± 90.4	581.7 ± 82.0
	Exercise	88.8 ± 14.3	78.9 ± 28.4	539.7 ± 102.1	596.9 ± 86.4

7.0 Discussion

This study examined whether a 20 minute, moderate intensity exercise bout positively influences cognitive processing in people with chronic stroke, using both behavioural (response time and accuracy) and EEG (P300 amplitude and latency) measures. Although behavioural performance was quite variable, our results indicate that the P300 amplitude was greater and the P300 latency was shorter 20 to 40 minutes after exercise. This suggests that attentional capacity and processing speed may be enhanced, or at least maintained, at a delay after exercise cessation. Our results suggest that even a single session of exercise may benefit cognitive functioning among chronic stroke patients. Future research should investigate whether pairing aerobic exercise with traditional rehabilitation tasks can improve rehabilitation outcomes.

7.1 Exercise and Electroencephalography

The P300 is an event related potential believed to reflect cognitive processing of a stimulus (Donchin, 1981). Its amplitude is thought to reflect the amount of attentional resources devoted to a particular task (Kramer & Strayer, 1988; Wickens, Kramer, Vanasse & Donchin, 1983). Our results suggest that people with chronic stroke can devote more attentional resources to an executive control task after a short delay post-exercise, as reflected by greater P300 amplitude at 40 minutes post exercise. The increase in P300 amplitude after exercise is in line with previous literature that suggests that moderate intensity exercise improves executive control among healthy adults; however there are differences in the time course of effects between that previously observed among healthy adults and what we observed among people who experienced a stroke (Hillman et al., 2003; Kamijo et al., 2004, 2007).

In contrast to previous literature (Hillman et al., 2003; Kamijo et al., 2004, 2007), P300 amplitude was not significantly different from before to immediately after exercise but was significantly different 40 minutes after exercise. As seen in Figure 6.1, P300 amplitude decreased across time points in the rest session while amplitude in the exercise session remained relatively stable across the time points. This suggests that exercise may not have an additive benefit to attentional processes among people with stroke per se, but that it may help to maintain attention over the course of 40 minutes or more. These findings are in line with a meta-analysis by Chang et al., (2012) that found that exercise was associated with negative effects on cognitive function when tests were administered within 10 minutes of exercise cessation, but found significant positive effects when tests were administered 11 or more minutes after the termination of exercise. Furthermore, it could be that the difference between rest and exercise increased between 20 and 40 minutes post-exercise and that only the latter was detectable with our small sample size. Further studies in populations with chronic stroke should include a larger sample size to determine if the P300 amplitude at other time points post-exercise are also significantly different from a rest condition. Additionally, future studies should examine whether positive effects to P300 amplitude remain beyond 40 minutes post-exercise.

The latency of the P300 is thought to represent the time it takes to evaluate a stimulus (Kutas, McCarthy & Donchin, 1977). In the current study, P300 latency was significantly shorter in central regions on the lesional side after a short delay post-exercise (20 minutes). This suggests that people with chronic stroke were able to evaluate stimuli more quickly after a brief delay post-exercise compared to at rest. These results are in line with previous literature which found P300 latency to be significantly reduced after aerobic exercise in both younger and older adults (Hillman et al., 2003; Kamijo et al., 2007; 2009) adults. However, the results are different

again because the shortened latency among people with stroke was after a 20 minute delay (Figure 6.4) rather than immediately after exercise cessation as in healthy adults. It is important to note that literature investigating the relationship between exercise and cognitive function thus far, has been limited in the examination of the time course of exercise effects. Future research in both healthy and clinical populations should examine the time course of the effect of exercise on cognitive function. It is possible that the time course of cognitive effects is altered by factors such as population studied and exercise dose.

One possible explanation for the difference in the time course of effects of exercise on both P300 amplitude and P300 latency is the relative strain of a given exercise intensity between populations. We hypothesize that the moderate intensity exercise prescription used in this study may have resulted in greater peripheral (muscular) and central (central nervous system) fatigue among our chronic stroke population compared to healthy adults. As mentioned in Section 2.6, patients with chronic stroke are likely to have lower fitness levels in comparison to age and sex-matched sedentary controls (Gordon et al., 2004; MacKay-Lyons & Makrides, 2004). Kamijo et al., (2007) suggested that hard intensity exercise among healthy adults may cancel beneficial effects on cognitive function that generally occur immediately after exercise of lower intensities. Whether the hard intensity elicited beneficial cognitive effects after a delay post-exercise was not investigated (Kamijo et al, 2007). It is possible that the moderate intensity used in the current study was more taxing to a chronic stroke group than among a group of healthy adults and thus, the positive effects of exercise on cognitive function were delayed until substantial recovery occurred. This is in agreement with a meta-analysis by Chang et al., (2012) which found that exercise intensity significantly altered the cognitive effects observed at 20 minutes post-exercise. Very light exercise negatively affected cognitive performance while moderate and hard exercise

positively affected cognitive performance at 20 minutes post-exercise (Chang et al., 2012). Future research should also be conducted to determine the effect of both exercise intensity and post-stroke fitness level on cognitive function as well as the time course of benefits.

The significant decrease in latency found on the lesional side rather than the contralesional side is also of interest. Perhaps damage to the lesional side allowed greater room for improvement, thus the quicker processing speed was evident. Future research among patients with chronic stroke should investigate the differential effect of exercise on lesional and contralesional sides of the brain. Additional regional differences were not evident within the small sample used with the exception of the F row. Amplitude of the F row was preferentially affected by exercise; reasoning for this preferential effect is further described in Section 7.4.

7.2 Exercise and Behavioural Performance

Unlike the P300 results, there was no significant difference in either accuracy or response time between exercise and rest sessions during a modified Eriksen Flanker task. This is in contrast to other studies that found response time was shorter after exercise among healthy adults (Kamijo et al., 2004, 2007, 2009). There are several possible reasons for a positive change to the P300 but a lack of significant alteration to behavioural measures. First, neuroelectric indices have been found to be more sensitive to aerobic exercise than behavioural measures (Hillman et al., 2003; Kamijo et al., 2007). Second, behavioural response may be too variable among people with chronic stroke, who typically have some amount of motor impairment. Further, some participants used their formerly non-dominant hand since the dominant side was affected by the stroke. This may also contribute to variability in motor execution and so a lack of sensitivity of behavioural measures. Due to the variability in performance, it may be that a larger sample size is needed to detect significant differences across sessions. Future research involving cognition in

stroke should enroll a larger sample or could decrease the variability in performance by using a chronic stroke population in which the unaffected side was the dominant side pre-stroke. Third, it is important to note that response time is a complex measure involving the time it takes for stimulus evaluation, response selection and response execution (Doucet & Stelmack, 1999). It has been suggested that these components may be differentially affected by exercise, in general as well as by exercise dose (Chang et al., 2012; Lambourne & Tomporowski, 2010). It is possible that these components may also be differentially affected by exercise after stroke. Since P300 latency reflects the time required for stimulus evaluation, but is unrelated to the response selection or execution (McCarthy & Donchin, 1981; Pfefferbaum, Ford, Johnson, Wenegrant, & Kopell, 1983), our results suggest the possibility that processing of a stimulus is positively affected by exercise but response selection and execution is either negatively or not affected.

Interestingly, accuracy became significantly worse with time between the pre-test and the 20 minute post-test across both sessions. This is in line with previous research in which accuracy was not influenced by one bout of aerobic exercise (Hillman et al., 2003; Kamijo et al., 2007; 2009). The decline in performance across time points however, was somewhat unexpected. Considering attention is a cognitive domain frequently affected post-stroke (Ballard et al. 2003; Cumming et al., 2012; Lesniak et al., 2008; Nys et al., 2005; Sachdev et al., 2004), it is possible that accuracy worsened over time simply due to an inability among participants to maintain attention allocation at later time points. This coincides with the significantly decreasing P300 amplitude over time observed during the rest session. Alternatively, since P300 amplitude was maintained during the exercise session, the worsening accuracy performance in the exercise session (as well as the rest session) may be due to poorer task execution rather than just a lack of attention over time.

7.3 Effect Modification by Congruency

Previous studies by Hillman et al., (2003) and Kamijo et al., (2007) found that P300 latency was shorter after exercise for incongruent stimuli but not for congruent stimuli among healthy young populations. In contrast, P300 latencies after both congruent and incongruent stimuli were significantly shortened after exercise in this study. The similar effect of exercise across conditions may be because of the age of the participants (generally older adults). Kamijo et al., (2009) found that the effect of exercise on P300 latency was also similar by condition among older adults but not young adults. The reason for an altered interaction between exercise and condition by age is unclear. Alternatively, it has been suggested that P300 latency is more influenced by exercise during tasks that require larger amounts of (inhibitory) executive control, such as the incongruent condition in our modified Flanker task (Kamijo et al., 2009). However, in this study, there were no differences in behavioural measures (accuracy or response time) between congruent and incongruent conditions, suggesting that there was no significant difference in difficulty between conditions among our participants. As a result, it is reasonable to suggest that exercise would influence both congruent and incongruent trials similarly, as seen in the current study.

Interestingly, the P300 latency across time for congruent stimuli appeared quite variable, yet there was no main effect of time (Figure 6.4 – Congruent). However, the latency for incongruent stimuli appeared to follow a more stable trend (Figure 6.4 – Incongruent); that is, latency increased with time in the rest session and decreased with time until 20 minutes after the exercise. Perhaps a larger sample size would further concatenate this pattern thus making the effect of exercise on P300 latency significantly different between conditions.

Despite there being a difference in response time based on congruency, the difference in accuracy with respect to congruency was not statistically significant. However, there was a trend for poorer accuracy in the incongruent condition which may have reached significance with a larger sample size ($p=0.11$). In prior studies, response time of incongruent stimuli has generally been longer and accuracy poorer in comparison to congruent stimuli suggesting that incongruent trials are more difficult (Hillman et al., 2003; Kamijo et al., 2007, 2009). In this study however, only response time but not accuracy was differentially affected by congruency. Considering the population used in this study has suffered previous stroke, perhaps the congruent trial was hard enough in itself and therefore the difference in difficulty between congruent and incongruent trials was minimal and not statistically evident.

Overall, differences between current and previous findings can likely or at least partially be explained by differences in population. This study tested chronic stroke patients rather than healthy adults and stroke patients may respond differently to exercise. One final suggestion to explain variations in current findings that was not previously mentioned, is the different exercise modality used. The aerobic exercise in the current study was completed on a recumbent stepper rather than more commonly used modalities such as a treadmill or stationary bike (Hillman et al., 2003; Kamijo et al., 2004; 2007; 2009). It seems unlikely that exercise on a recumbent stepper affected the results because the stepper is very similar to a stationary bike; however little is currently known about the effect of exercise type (modality) on cognition.

7.4 Potential Mechanisms

A definitive mechanism to explain improvements in cognitive (executive) function after a single session of aerobic exercise remains elusive. In the current study, it was likely a combination of increased cerebral blood flow and increased levels of brain neurotransmitters that

influenced the P300 and improved cognitive function. Despite the positive role BDNF may play on synaptic transmission, literature suggests that the time course is either very short for peripheral levels in humans or very delayed for central levels in rats. These time courses do not match the time course of effects observed in the current study. In contrast, both increases in cerebral blood flow and increases in catecholamine concentrations show a prolonged response after exercise cessation, similar to the positive effects in P300 amplitude and latency observed in this study (Goekint et al,, 2012; MacIntosh et al., 2014; Meeusen et al., 1997; Pagliari & Peyrin, 1995; Smith et al., 2010). Although plasma catecholamine levels generally return to baseline by 30 minutes post-exercise (Galbo et al., 1975), levels of brain neurotransmitters such as NE, DA and GLU remain significantly elevated anywhere from 20 to 120 minutes after exercise cessation (Goekint et al., 2012; Meeusen et al., 1997; Pagliari & Peyrin, 1995). An increased concentration of these neurotransmitters over this time period also suggests that increased synthesis and metabolism occurs over this time period (Brown et al., 1979; Brown & Van Huss, 1973; de Castro & Duncan, 1985). This is in line with the time course of enhanced P300 amplitude and latency observed at 20 to 40 minutes post-exercise in this study. It is possible that increases in cerebral blood flow are linked to levels of neurotransmitters. Increases in cerebral blood flow could increase the availability of resources or could be driven by the increased production and metabolism of neurotransmitters. Therefore, these two mechanisms may work together to produce improvements in cognitive function after aerobic exercise.

Additional evidence for the contribution of NE to improved cognitive function in the current study can be seen by similarities in important regions. Previous literature suggests NE innervation to the inferior parietal and frontal cortices is high (Nieuwenhuis et al., 2005). The

largest P300 amplitudes in this study were found at the Pz electrode site while the greatest effects of P300 amplitude were found in the frontal region.

8.0 Strengths and Limitations

A major strength of this study was its novelty in population and measures. This study was the first to examine neuroelectric indices using EEG after a single session of aerobic exercise in a population with chronic stroke. EEG measures reflecting cognitive processing are more sensitive than behavioural performance, especially in the context of measuring the effect of exercise on cognitive function. It was also the first study to specifically examine the time course of cognitive effects after aerobic exercise, whereas most previous studies have only measured at one time point post-exercise. Due to the small sample size however, our results should be considered preliminary. It is possible that additional differences or a lack of differences may be found with a larger sample size. A second limitation is that some participants had low accuracy during the flanker task; yet when the results were examined closely, most of the errors were due to very slow response times that did not register as opposed to true errors. Accuracy was also found to be greatest before the interventions, which suggests the task was initially understood by the participants but that performance worsened over time. We believe this is to be expected in persons who have had a stroke because of difficulties maintaining attention. Another limitation to this study is that we only used one cognitive task (a modified Flanker task) and therefore only tested one aspect of executive function – inhibition. Future research should be conducted in chronic stroke populations to determine if exercise can improve other aspects of executive function. Finally, we only measured up to 40 minutes post-exercise. Since the P300 amplitude improvements were maximal at 40 minutes post-exercise, it is possible that peak effects may occur after our testing period. Future EEG research should be conducted beyond 40 minutes post-exercise to determine the full time course of the lasting effects of exercise on cognitive processing in a chronic stroke population.

It is also important to note two particular situations. One participant was actively involved in an exercise rehabilitation program; however, P300 measures taken pre-intervention on both the exercise and rest days were compared and were not significantly different from each other. Furthermore, this participant completed the exercise session first, so if the exercise rehabilitation affected cognitive function, it would have likely reduced the difference between sessions. In addition, it is unknown at this point in time whether fitness affects the cognitive response to one bout of aerobic exercise. Another participant had to complete the exercise and rest sessions three days apart rather than two weeks apart; however the exercise session was again completed first, so any learning effects would likely minimize the differences between sessions.

9.0 Conclusion and Future Directions

We found that exercise exerts its greatest effect on P300 latency and amplitude after a 20 to 40 minute delay among people with chronic stroke. It appears as though exercise allows for the maintenance of attentional resources which otherwise declined over time, and shortened cognitive processing speed which otherwise became slower with time during a task of executive control. These findings provide preliminary evidence that one bout of moderate intensity aerobic exercise on a recumbent stepper may facilitate and/or maintain task appropriate attentional resources and shorten cognitive processing time after a delay post-exercise, thus benefitting executive control functions among those living with chronic stroke. If exercise provides a tool for maintaining attentional capacity and shortening cognitive processing speed, it may be that performing an exercise session prior to traditional rehabilitation could improve outcomes and/or maximize the time for effective therapy for at least 40 minutes post-exercise. Future research should examine the effect of various exercise doses on cognitive function as well as whether pairing exercise with rehabilitation improves clinical outcomes.

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Appendix A: Consent Form

UNIVERSITY OF WATERLOO

INFORMATION CONSENT FORM

Physical Activity and Cognitive Function

Investigators
Laura Middleton, PhD, University of Waterloo, Department of Kinesiology, 519-888-4567 Ext. 33045
Karli Swatridge, MSc. Candidate, University of Waterloo, Department of Kinesiology, 519-888-4567 Ext

INTRODUCTION
You are being invited to take part in a research study. Before agreeing to participate in this study, it is important that you read the study procedures. The following information describes the purpose, procedures, benefits, discomforts, risks and precautions associated with this study. It also describes your right to refuse to participate or withdraw from the study at any time. In order to decide whether you wish to participate in this research study, you should be aware of its risks and benefits to be able to make an informed decision. This is known as the informed consent process. Please ask the study staff to explain any details that are unclear before signing this consent form. Make sure all your questions have been answered to your satisfaction before signing this form.

WHAT IS THE PURPOSE OF THIS STUDY?
Physical activity is recommended to benefit physical health. Growing research suggests that physical activity is not only associated with physical health but also thinking abilities. The purpose of this study is to determine how physical activity affects your thinking abilities and brain health after a stroke.

ELIGIBILITY
You are eligible for this study if you experienced a stroke 6 or more months ago. You are ineligible if you have an unstable medical condition that could make exercise unsafe or have a condition that would interfere with the study procedures. These include:

- History of heart failure or heart implant
- Hospitalization for heart attack or heart surgery within 2 years
- Uncontrolled diabetes (your blood sugar levels are not well regulated by medicine, diet or exercise)
- Uncontrolled hypertension (your blood pressure is not well regulated with or without medicine)
- Drop in blood pressure when you rise from a seated position (symptoms include dizziness and feeling like you will faint)
- Neurological conditions including epilepsy, Parkinson's disease, or dementia
- Have chronic obstructive pulmonary disease
- Have musculoskeletal impairments that cause too more pain during exercise than is tolerable
- You have a history of allergies to electrode gel or adhesive

Cap used to monitor your brain function.

WHAT WILL YOU BE ASKED TO DO?

If you agree to participate, you will be asked to attend three sessions in a kinesiology lab at the University of Waterloo. These visits will be 1.5 to 2 hours in duration. These visits will take place approximately 2 weeks apart. You will be carefully monitored during each session.

Prior to the first visit, you will sign this consent form and complete an exercise screening form. You will have to take the exercise screening form to your doctor to fill it out (or it can be faxed to your doctor by us). If you are charged for this service, we will reimburse you for the cost.

At the first visit, you will arrive with a completed ParMED-X form signed by your physician. You will then work with a researcher to complete a 10 minute test which assesses general brain function. After this short test, you will be given some time to practice a series of thinking tasks. These tasks are done on a computer and involve determining whether a picture is facing right or left, remembering and identifying numbers and reacting as quickly as possible. Errors are normal on all of the tests and should not be taken as a reflection of your cognitive abilities!

You will then perform a multi-stage exercise test on a recumbent stepper (similar to a recumbent bike). You will perform 2 minutes at a low intensity that should feel as difficult as walking. You will then perform 2 minutes at a slightly higher intensity that will make your heart beat faster and your breathing rate increase. This increase will continue every two minutes for up to 12 minutes. Your heart rate will be measured with a chest strap throughout and we will check your blood pressure every 5 minutes. We will also monitor the air you breathe in and out using a mask. This test will not push you to your maximum abilities but you will likely be fatigued after the session. If you feel any unusual discomfort or pain or if you feel dizzy, faint, or light headed during this test, inform the researcher immediately and the test will be stopped. You will be supervised by personnel with CPR training for emergency purposes. This first session will take about 1 hour.

You will return to the laboratory for two other sessions. In one of the sessions you will sit on the recumbent stepper for 20 minutes. In the other session you will exercise on the recumbent stepper for 20 minutes. How hard you exercise in this session will be carefully set and monitored. It may be similar to walking or a little harder. You will be free to stop at any time. Before and after the exercise, you will perform a series of thinking tasks while your brain activity is monitored. You will wear a cap with electrodes that monitor your brain activity during these tests. A picture of the cap is shown above. The cap contains many disks that sit on the surface of your scalp. Prior to testing, we need to clean the sites underneath each of the disks and move the hair out of the way. This is done using a disposable blunt syringe, which is not sharp and is about

as wide as a pen tip. This blunt syringe is also used to squirt a small amount of gel onto your scalp to improve the signal from your brain activity. Both of these sessions will take approximately 1.5 - 2 hours. You will be provided a towel and shampoo to wash your hair, if you wish, at the end of these study sessions.

HOW MUCH TIME WILL IT TAKE?
Your first visit will be approximately 1 hour.
Your second and third visits will be approximately 1.5 - 2 hours each.

PARTICIPATION
If you choose to participate, we recommend wearing light, comfortable clothing and running shoes to the study sessions.

Participation in this study is entirely voluntary and you may refuse to participate or withdraw at any time by informing the researcher or research assistants. You may also decline to answer question(s) or stop taking part in the study tasks at any time by notifying the researcher. Likewise, the researchers may also stop participation of anyone in the study at any time. If we learn any new information that might affect your desire to participate or decision to remain in the study, you will be told of this.

LOCATION
All study sessions will be performed in the Brain and Body Lab which is in the B.C. Matthews Hall, Room 1015 at the University of Waterloo.

RISKS
You may experience temporary muscle fatigue or soreness from the exercise. Exercise intensities will be low to moderate, reducing the risk of fatigue.

During exercise, there is always a small chance that chest pain (cardiac ischemia) or heart beat irregularity (arrhythmia) will occur. You will only be included in the study if you are considered to be at low risk for such events. In addition, we will stop the exercise if you report chest pain, shortness of breath, drowsiness, feeling faint, dizziness or lightheadedness. Monitoring of heart rate and blood pressure will be done continuously to detect any abnormal changes. You will be under direct supervision for the entire study to ensure your safety.

You may experience mild pain or discomfort when we clean your skin using abrasive gel so that we can monitor your brain activity. If you have sensitive skin, you may develop a slight reddening from the adhesive used to affix some electrodes to the skin. Your head may also be slightly sore from wearing the EEG cap. Electrode gel will get into your hair as a result of the EEG cap, but soap, shampoo, conditioner and towels will be provided if you wish to wash your hair in a nearby changing facility. Any person with allergies or sensitivities to alcohol will be excluded from this study. The researcher will ask you if you have any known allergies or sensitivities before beginning the procedures.

BENEFITS
By participating in this study, you will benefit by furthering your knowledge and understanding of experimental procedures commonly used in neuroscience research. Your help will contribute to our knowledge on the benefits of aerobic exercise to brain health. This study may provide insight for future

research on stroke rehabilitation and prevention of cognitive impairment, particularly research on neuroplasticity (the brain's ability to adapt).

CONFIDENTIALITY AND SECURITY OF INFORMATION

Your identity will be kept confidential and will not be passed to a third party. Only the researchers associated with the study (Dr. Middleton, MSc. Student Karli Swatridge and associated research assistants) will have access to the data. The collected data will be coded with participant numbers (not names) and will be kept in a locked file cabinet in Burt Matthews Hall room 1114 or on a password-protected computer for seven years after publication. After this time, all paper copies will be shredded and computer disks erased.

QUESTIONS

Any questions with regard to this research should be directed to Karli Swatridge, 519-888-4567 Ext. 38548 or Laura Middleton, 519-888-4567 Ext. 33045.

ETHICS CLEARANCE

This study has been reviewed by the Office of Research Ethics at the University of Waterloo; however the final decision about participation is yours. If you have any comments or concerns resulting from your participation in this study, you may contact the Office of Research Ethics, 519-888-4567 Ext. 36005.

UNIVERSITY OF WATERLOO
L Middleton, K. Swatridge

CONSENT FORM

Physical Activity and Cognitive Function

I have been informed of the aim of this study, and have read the INFORMATION AND CONSENT FORM. I am aware that I am under no obligation to take part and may withdraw from the study at any time.

I am aware that the researchers will be asking me questions concerning my health. This information will remain confidential and I will be free to refuse to reply to any question that I prefer not to answer.

I am aware that I am free to ask questions and to withdraw from this study at any time. I am also aware that, if I feel uncomfortable during exercise, I may ask the researcher to stop it immediately.

I am aware that by signing this consent form, I am not waiving my legal rights, nor does it relieve the investigators or involved institution from their legal and professional responsibilities.

I agree to take part in the study. I will receive a copy of the signed consent form.

_____
PARTICIPANT NAME

_____
PARTICIPANT SIGNATURE

_____
LOCATION

_____
DATE

_____
WITNESS

Appendix B: Chedoke-McMaster Stroke Assessment (Arm and Leg)

IMPAIRMENT INVENTORY: STAGE OF ARM

Standard Starting Position: Sitting with the forearm in the lap or supported on a pillow in the lap in a neutral position, wrist at 0° and fingers slightly flexed. Sitting either unsupported over the side of the bed or plinth, or supported in a chair or wheelchair. Feet should be supported. Encourage good sitting posture during testing (ie. with hips and knees at 90°). Start the assessment at Stage 3.

STAGE 1
Unable to demonstrate at least two of the Stage 2 tasks.

STAGE 2 *Support the limb as necessary while facilitating the movements.*
Task 1: Resistance to passive shoulder abduction or elbow extension
Position: Standard starting position.
Instruction: "Let me move your arm."
Method: Choose either a) or b):
a) Abduct and adduct shoulder 5 times with sufficient speed of passive movement to elicit a stretch reflex. Do not exceed 70° of abduction. Feel for resistance to passive movement and watch for active contraction of pectoral muscles. Do with care, respecting pain.
b) Flex and extend elbow 5 times with sufficient speed of passive movement to elicit a stretch reflex.
Required: Feel for resistance to passive movement and watch for active contraction of the stretched muscle.
Task 2: Facilitated elbow extension
Position: Standard starting position.
Instruction: "Straighten your elbow and try to touch your opposite knee."
Method: Facilitate a contraction of the elbow extensors.
Required: Some observed active elbow extension.
Task 3: Facilitated elbow flexion
Position: Standard starting position.
Instruction: "Bend your elbow."
Method: Facilitate a contraction of the elbow flexors.

STAGE 3
Task 1: Touch opposite knee
Position: Standard starting position.
Instruction: "Straighten your elbow and try to touch your opposite knee."
Required: Active shoulder adduction and full elbow extension with palm facing down.
Permitted: The wrist may be supported in a neutral position so that it does not interfere with arm extension.
Task 2: Touch chin
Position: Standard starting position.

Instruction: "Touch your chin with your hand."
Required: Sufficient elbow flexion for any part of the hand to touch the chin. Movement in synergy is permissible.
Not permitted: Flexion of head

Task 3: Shoulder shrugging greater than half range

Position: Standard starting position.
Instruction: "Shrug both shoulders up towards your ears."
Required: Active scapular elevation greater than half range. Movement in synergy is permissible.

STAGE 4

Task 1: Extension synergy, then flexion synergy

Position: Standard starting position.
Instruction: "Reach across and touch your opposite knee with your elbow straight, then without stopping, touch the ear on your weak side, keeping your elbow up."
Required: Shoulder adduction and full elbow extension to touch or pass the top of the opposite knee with full internal rotation of the shoulder and pronation of the forearm. Then without stopping the shoulder should attain at least 90° of abduction with 0° horizontal flexion and some external rotation when the hand touches the ear. The forearm may be either pronated or supinated.
Don't accept: Prolonged pause between synergies.

Task 2: Shoulder flexion to 90°

Position: Standard starting position
Instruction: "Keep your elbow straight throughout movement, and lift your arm up to shoulder height."
Required: Shoulder flexion to 90° with full elbow extension. Forearm may be pronated.
Don't accept: Shoulder abduction, scapular elevation or elbow flexion.

Task 3: Supination then pronation

Position: Elbow at side with 90° elbow flexion.
Instruction: "Keep your elbow at your side, and turn your palm up and then down."
Required: Full supination and full pronation. Elbow remains at side of trunk.
Don't accept: Compensatory movement of trunk.

STAGE 5

Task 1: Flexion synergy, then extension synergy

Position: Standard starting position.
Instruction: "Touch the ear on your weak side, keeping your elbow up, and then without stopping reach towards your opposite knee, finishing with your elbow straight."
Method: Watch for 90° of shoulder abduction with 0° horizontal flexion and external rotation to touch the ear with any part of the hand. The elbow may be flexed with either pronation or supination. Touch the opposite knee while fully extending the elbow and adducting and internally rotating the shoulder with pronation of the forearm so that the palm faces down.
Required: Smooth controlled reversal between synergies, and full elbow extension

Task 2: Shoulder abduction to 90° with pronation

Position: Standard starting position.
Instruction: "Lift your arm out to the side, keeping your elbow straight and your palm down."
Required: Shoulder abduction 90° with full elbow extension. Forearm must be pronated.

Wrist control is not necessary.
Don't accept: Compensatory movements: trunk side flexion, scapular elevation, shoulder flexion, or elbow flexion.

Task 3: Pronation then supination

Position: Shoulder flexion to 90°, arm in midposition.
Instruction: "Keep your elbow straight, and turn your palm down and then up."
Required: Full pronation, full supination (with or without internal and external rotation of shoulder) and full elbow extension with 90° of shoulder flexion.
Don't accept: Compensatory trunk movements or elbow flexion. Loss of shoulder flexion. .

STAGE 6:

Task 1: Hand from knee to forehead 5 times in 5 seconds

Position: Standard starting position.
Instruction: "Touch your forehead and your weak knee as quickly as possible."
Method: Count the knee to forehead repetitions in 5 seconds. Note that some part of the hand or wrist touches the knee and the forehead on each repetition.
Required: Smoothness of movement.
Don't accept: To lower head or raise knee.

Task 2: Trace a vertical figure 8

Position: Shoulder flexion to 90°.
Instruction: "Draw a large "figure 8" keeping your elbow straight."
Required: The figure 8 is drawn smoothly, both above and below 90° of shoulder flexion.
The elbow must be straight throughout the movement. Finish with the arm at shoulder level. The circles should be 20-30 centimeters (8-12 inches) in diameter.
Don't accept: A small pattern, or compensatory trunk movements to achieve the pattern, elbow flexion through any part of the pattern, or a jerky pattern.

Task 3: Raise arm overhead with full supination

Position: Arm resting at side of body.
Instruction: "Raise your arm over your head keeping your elbow straight and finish with your palm facing backwards."
Required: Full shoulder flexion, elbow extension and supination. Elbow extended through the movement.
Don't accept: Shoulder abduction, elbow flexion, less than full supination or any compensatory trunk movements.

STAGE 7

Task l: Clap hands overhead, then clap hands behind back 3 times in 5 seconds

Position: Arms at side of body while standing (or sitting on stool).
Instruction: "Clap your hands above your head, then behind your back as quickly as possible."
Method: One movement consists of clapping hand overhead and behind back. Time the number of movements performed in 5 seconds. Listen for clap overhead while watching for the coordinated movement.
Required: Smooth coordinated movement with shoulder flexion range of 160-180°.
Don't accept: Clapping hands in front of face, not overhead.

Task 2: Scissor in front 3 times in 5 seconds

Position: Shoulder flexion to 90°, elbows extended and forearms pronated.

Instruction: "Keep your elbows straight and your palms down. Cross your arms in front of you, alternating the arm that crosses on top. Repeat the over/under movement 3 times."
Required: Shoulders remain held in 90° flexion throughout the movement with elbows extended and forearms pronated. Equal range (shoulder width) and speed of crossovers. Smooth coordinated movement.
Don't accept: Stopping between repetitions.

Task 3: Resisted shoulder external rotation

Position: Both elbows at side with 90° elbow flexion.
Instruction: "Keep your elbows at your side. Tighten your muscles and don't let me push your arms in"
Method: Place hands on client's forearms. Instruct client as above and apply resistance to external rotation. Maintain resistance for 3 seconds.
Required: Equal strength bilaterally.

IMPAIRMENT INVENTORY: STAGE OF LEG

Standard starting position: Lying on back with knees bent and feet flat, with hands resting on stomach, shoes and socks off, and pants rolled up. Start assessment at Stage 4.

STAGE 1

Unable to demonstrate at least two of the Stage 2 tasks.

STAGE 2

Task 1: Resistance to passive hip or knee flexion

Position: Standard starting position, with limb supported as necessary.
Instruction: "Let me move your leg."
Method: Choose either a) or b):
a) flex and extend hip 5 times with sufficient speed of passive movement to elicit stretch reflex. Feel for resistance to passive movement and watch for an active contraction of hip flexors.
b) flex and extend knee 5 times with sufficient speed of passive movement to elicit stretch reflex. Feel for resistance to passive movement and watch for an active contraction of the quadriceps.

Task 2: Facilitated hip flexion

Position: Standard starting position.
Instruction: "Bend your leg towards your chest."
Method: Facilitate a contraction of the hip flexors.
Required: Some active hip flexion.

Task 3: Facilitated extension

Position: Standard starting position.
Instruction: "Straighten your leg out."
Method: Facilitate a contraction of hip and knee extensors.
Required: Some active contraction of hip or knee extensors.

STAGE 3

Task 1: Adduction to neutral

Position: Standard starting position with weak leg abducted (30-45°).
Instruction: "Bring your weak knee into the middle."
Method: Adduction of weak leg to neutral. Foot may be stabilized.

Task 2: Hip flexion to 90°

Position: Standard starting position.
Instruction: "Bend your leg up towards your chest."
Required: Hip flexion to 90° (hip abduction and/or pelvic tilt are permitted).

Task 3: Full extension

Position: Standard starting position. Leg may be stabilized.
Instruction: "Straighten your leg out."
Method: Full active hip and knee extension. Gravity may assist with the movement. Adduction and internal rotation are not required, but are permitted.

STAGE 4

Task 1: Hip flexion to 90° then extension synergy

Position: Standard starting position. The unaffected leg remains in flexion during this task.
Instruction: "Bend your leg up towards your chest, and out to the side. Then without stopping, straighten your leg out, crossing your weak leg over the mid-line."
Required: Hip and knee flexion to 90°, hip abduction to 45°, and external rotation at least to neutral during the flexion component. Full extension of hip and knee with sufficient hip internal rotation and adduction to cross the weak foot over the midline. No stopping between synergies.
Don't accept: Prolonged pause between synergies.

Task 2: Bridging hips with equal weight bearing

Position: Standard starting position.
Instruction: "Lift your hips off the bed pushing equally with both feet."
Method: Test for equal weight bearing by trying to displace the weak foot.
Required: Hip extension and weight bearing equal bilaterally. Pelvis aligned.
Don't accept: The use of a non-slip material under the weak foot.

Task 3: Knee flexion beyond 100°

Position: Sitting, hips and knees flexed to 90° and feet supported.
Instruction: "Bend your knee back as far as you can."
Required: Knee flexion greater than 100°.
Acceptable: Part of the foot can remain in contact with the floor.
Don't accept: Excessive trunk movement.

STAGE 5

Task 1: Extension synergy, then flexion synergy

Position: Standard starting position. The unaffected leg remains in flexion during this task.
Instruction: "Straighten your leg out crossing your weak leg over the mid-line, then without stopping, bring your weak leg up towards your chest and out to the side."
Required: Full extension of hip and knee with sufficient hip internal rotation and adduction to cross weak foot over the mid-line. Hip and knee flexion to 90°, hip abduction to 45° with external rotation at least to neutral. Smooth transition between synergies.

Task 2: Raise thigh off bed

Position: Sitting, hips and knees flexed to 90°. Feet on floor.
Instruction: "Lift your thigh off the bed."

Required: Active hip flexion through inner range so that the thigh clears the bed.
Don't accept: External rotation of hip, compensating trunk movements, or use of hands.

Task 3: Hip extension with knee flexion

Position: Standing on strong leg with light support.
Instruction: "Take your leg back, keep it there, then lift your heel towards your bottom."
Method: Therapist may provide light support for balance.
Required: Hip extension to 0° with enough knee flexion to raise the foot off the floor.
Don't accept: Compensatory trunk movements or weight bearing through the support offered by the therapist. Less than neutral hip extension while flexing knee.

STAGE 6

Task 1: Lift foot off floor 5 times in 5 seconds

Position: Sitting with hips and knees at 90°, feet supported.
Instruction**:** "Lift your thigh off the bed and stamp the floor with your whole foot 5 times."
Method: Count the number of times the foot taps the floor in 5 seconds.
Required: 90°knee flexion. Each repetition should be of equal amplitude.
Don't accept: Compensatory trunk or hip movements, less than 90°knee flexion.

Task 2: Full range internal rotation

Position: Sitting with hip and knees at 90_o, feet supported.
Instruction: "Keep your knees together and spread your ankles apart."
Method: It is permissible to hold on to the bed.
Required: Full range of internal rotation (compare to other side), no compensatory trunk movements. Feet should come off the support.
Don't accept: Hip flexion or movement in synergy

Task 3: Trace a pattern: forward, side, back, return

Position: Standing on strong leg with light support.
Instruction: "Trace the shape of a triangle on the floor: forward, side, back, return. Keep your forefoot on the floor and keep your knee straight."
Method: Therapist may provide light support for balance.
Required: Smooth, coordinated hip flexion, abduction and extension while keeping the knee extended.
Don't accept: Weight bearing through support, jerky movements or knee flexion when the leg is abducting or extending.
Acceptable: Knee flexion is permitted when the limb is returning to the neutral position from hip extension.

STAGE 7

Task 1: Rapid high stepping 10 times in 5 seconds

Position: Standing unsupported.
Instruction: "Quickly march on the spot lifting your legs up high."
Method: Count 10 high steps, 5 with each leg, in 5 seconds.
Required: Consistent step height with at least 45^o of hip flexion.

Task 2: Trace a pattern quickly; forward, side, back, return. Reverse pattern

Position: Standing with light support**.**
Instruction: "Quickly trace a shape of a triangle on the floor and without stopping, reverse the pattern. Keep your forefoot on the floor and keep your knee straight**.**"

Method: Movement consists of hip flexion, abduction and extension while keeping knee extended.
Required: Smooth, coordinated, movement with a rapid reversal.
Acceptable: Knee flexion is permitted when the limb is returning to the neutral position from hip extension.

Task 3: Hop on weak leg

Position: Standing on weak leg with light support.
Instruction: "Hop on your weak foot."
Method: Therapist may provide light support for balance.
Required: Sufficient clearance so that the whole foot is off the floor. Ankle stability.
Don't accept: Weight bearing through support. Excessive trunk movements.

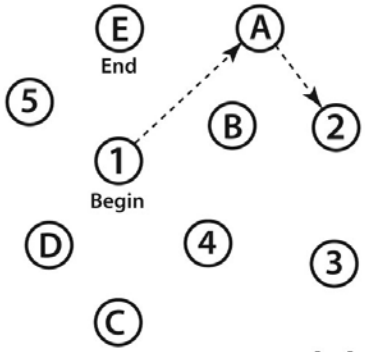
Administration instructions for the arm and leg components of the Chedoke-McMaster Stroke Assessment taken and modified from, CMSA (2007). The entire assessment can be found at CMSA (2007).

Appendix C: Montreal Cognitive Assessment (MoCA)

MONTREAL COGNITIVE ASSESSMENT (MOCA)
Version 7.1 Original Version

NAME :
Education : Date of birth :
Sex : DATE :

VISUOSPATIAL / EXECUTIVE — POINTS



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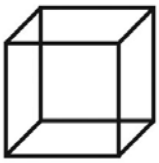


[ ] [ ]

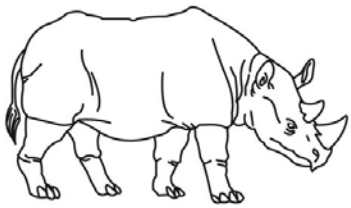
Draw CLOCK (Ten past eleven) (3 points)

[ ] Contour [ ] Numbers [ ] Hands

__/5

NAMING

[ ]



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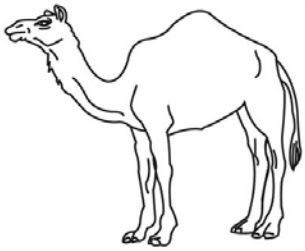

[ ]

__/3

MEMORY Read list of words, subject must repeat them. Do 2 trials, even if 1st trial is successful. Do a recall after 5 minutes.

	FACE	VELVET	CHURCH	DAISY	RED
1st trial					
2nd trial					

No points

ATTENTION Read list of digits (1 digit/ sec.).

Subject has to repeat them in the forward order [ ] 2 1 8 5 4

Subject has to repeat them in the backward order [ ] 7 4 2

__/2

Read list of letters. The subject must tap with his hand at each letter A. No points if ≥ 2 errors

[ ] F B A C M N A A J K L B A F A K D E A A A J A M O F A A B

__/1

Serial 7 subtraction starting at 100 [ ] 93 [ ] 86 [ ] 79 [ ] 72 [ ] 65

4 or 5 correct subtractions: **3 pts**, 2 or 3 correct: **2 pts**, 1 correct: **1 pt**, 0 correct: **0 pt**

__/3

LANGUAGE Repeat : I only know that John is the one to help today. [ ]

The cat always hid under the couch when dogs were in the room. [ ]

__/2

Fluency / Name maximum number of words in one minute that begin with the letter F [ ] _____ (N ≥ 11 words)

__/1

ABSTRACTION Similarity between e.g. banana - orange = fruit [ ] train – bicycle [ ] watch - ruler

__/2

DELAYED RECALL

	Has to recall words WITH NO CUE	FACE [ ]	VELVET [ ]	CHURCH [ ]	DAISY [ ]	RED [ ]	Points for UNCUED recall only
Optional	Category cue						
	Multiple choice cue						

__/5

ORIENTATION [ ] Date [ ] Month [ ] Year [ ] Day [ ] Place [ ] City

__/6

© Z.Nasreddine MD www.mocatest.org Normal ≥ 26 / 30

TOTAL __/30

Add 1 point if ≤ 12 yr edu

Administered by: _____

MoCA, taken from Nasreddine (2013).

Appendix D: Submaximal Exercise Test Protocol

Modified Total-Body Recumbent Stepper Exercise Test Protocol

Level	Duration (min)	Stepping Cadence (steps/min)
1	2	80
2	2	80
3	2	80
4	2	80
5	2	80
6	2	80
7	2	80
8	2	80
9	2	80
10	2	80

Table has been modified from Billinger et al. (2008). It outlines the stepping cadence and duration of each stage/level in the submaximal exercise protocol for stroke patients on a recumbent stepper used in this study.

Appendix E: Borg Scale of Rating of Perceived Exertion

BORG RATING OF PERCEIVED EXERTION (RPE) SCALE

Number rating	Verbal rating	Example
6		No effort at all. Sitting and doing nothing.
7	Very, very light	Your effort is just noticeable.
8		
9	Very light	Walking slowly at your own pace.
10		Light effort.
11	Fairly light	Still feels like you have enough energy to continue exercising.
12		
13	Somewhat hard	
14		Strong effort needed.
15	Hard	
16		Very strong effort needed.
17	Very hard	You can still go on but you really have to push yourself. It feels very heavy and you're very tired.
18		
19	Very, very hard	For most people, this is the most strenuous exercise they have ever done. Almost maximal effort.
20		Absolute maximal effort (highest possible). Exhaustion.

Table taken from PAL (2013) supplied by the Canadian Society of Exercise Physiology.

Appendix F: Modified Eriksen Flanker Task

Condition	Display	Correct Answer
Incongruent Right	< < > < <	Right click
Incongruent Left	> > < > >	Left click
Congruent Right	> > > > >	Right click
Congruent Left	< < < < <	Left click

This table illustrates each of the four potential conditions of the modified Eriksen Flanker task and the corresponding correct answer.

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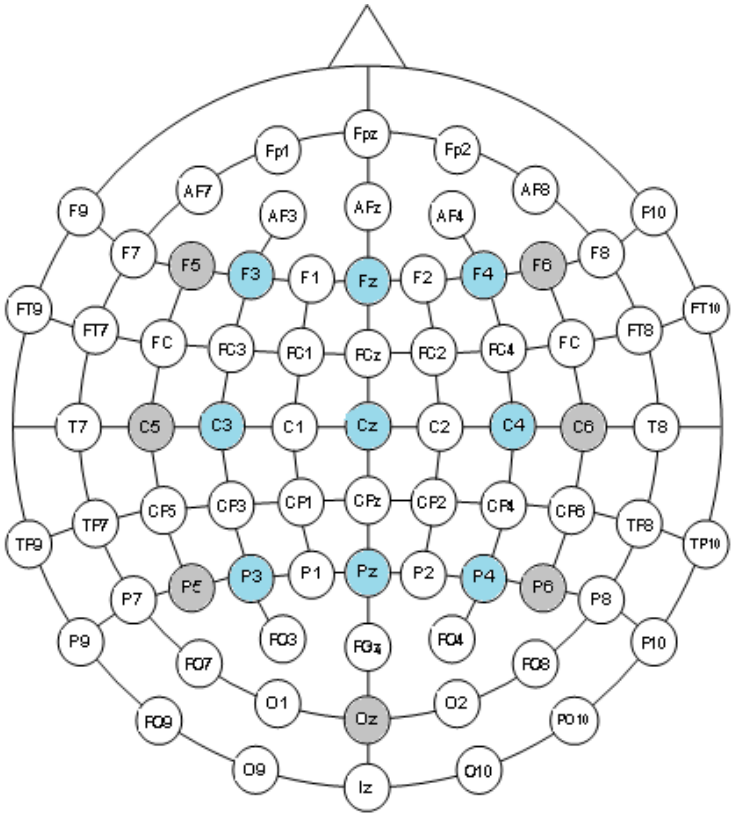
Appendix G: Diagram of Electrodes



This is a schematic of the electrode placement on the *QuickCap*. All shaded electrodes (blue and grey) were collected. The electrodes used for analyses are shaded in blue.

Appendix H: Formulas

Age Predictive Maximal Heart Rate (HRmax) Equations
(Brawner et al., 2004; Tanaka, Monahan & Seals, 2001)

For individuals ≥ 40 years
HRmax (bpm) = 208 – (0.7 × age)

For individuals on a β-blocker
HRmax (bpm) = 164 – (0.7 × age)

Heart Rate Reserve Method to determine Target Heart Rate
(ACSM, 2013)

Target Heart Rate = [(% exercise intensity) × HRmax – HRrest)] + HR rest

Appendix I: Sample Target Heart Rate Calculation

Participant Characteristics:
Age = 72
Resting Heart Rate = 75 beats/minute

Predictive HRmax

- Participant is > 65 years
- HRmax (bpm) = 208 – (0.7 × age)
  = 208 – (0.7 × 72)
  = 157.6 bpm

Target Heart Rate using 45-55% HRR

- 45 % Target Heart Rate = [% exercise intensity × (HRmax – HRrest)] + HR rest
  = [0.45 × (157.6 – 75)] + 75
  = 112.17 bpm

- 55% Target Heart Rate = [% exercise intensity × (HRmax – HRrest)] + HR rest
  = [0.55 × (157.6 – 75)] + 75
  = 120.43 bpm

Therefore, the target heart for this exercise session would be between the range of 112 and 120 beats per minute (bpm).